CHAPTER 11

NEUROLOGICAL ASSESSMENT

INTRODUCTION

Background

The frequent association of subjective neurological symptoms subsequent to herbicide exposure has driven much of the research on the potential neurotoxicity of dioxin. Studies of industrial accidents have demonstrated that the mixed sensorimotor neuropathy associated with extreme chlorophenol toxicity is reversible and that there is little scientific evidence to date for any chronic central or peripheral neurological disease in humans associated with low-level 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD, or dioxin) exposure. Neurobehavioral endpoints in humans, the subject of intensive investigation in this and other studies of Vietnam veterans, are considered separately in Chapter 12, Psychological Assessment.

Most of the basic research in animal models has focused on the neurobehavioral toxicity of 2,4-D and 2,4,5-T rather than TCDD. In rats (1-4), mice (5), and rabbits (6), perinatal exposure to 2,4-D induced neurobehavioral dysfunction associated with alterations in the concentrations of several central nervous system (CNS) neurotransmitters. In another series of experiments, the neurobehavioral effects of exposure to an ester of 2,4-D were found to be rapidly reversible, and a cellular rather than biochemical basis for the tolerance that developed with repeated injections was proposed by the authors (7-9).

A few studies have investigated the neurotoxic effects of TCDD in laboratory animals. In one experiment (10), the intracerebroventricular administration of TCDD proved far more toxic than the subcutaneous route in producing a wasting syndrome in rats though specific neurological indices were not examined. In another study, the neuromuscular effects associated with acute lethal doses of TCDD in rats were primarily on muscle tissue rather than peripheral nerves (11). A recently reported experiment, which included electrophysiologic studies, found that TCDD administered intraperitoneally in low doses to rats caused dose-dependent and statistically significant reductions in sciatic nerve motor and sensory conduction velocities consistent with a toxic polyneuropathy (12).

In humans, there is only circumstantial evidence linking 2,4-D exposure to neurotoxicity and the arguments against a causal relationship have been summarized in a recent review article (13). A host of subjective neurological symptoms has been reported following TCDD exposure and grouped generically under the diagnosis of "neurasthenia." Numerous studies have been published describing neurological sequelae in populations occupationally exposed to TCDD (14-21), environmental contamination (22-26), and industrial accidents (26-33). The 1976 chemical explosion in Seveso, Italy, provided a basis for longitudinal studies on the exposed population. Several of these studies have included neurological indices. One report included objective data derived from comprehensive neurological examination and electrophysiologic testing performed 7 years after the accident (28). In this report, 152 subjects with chloracne, a marker for high level dioxin exposure, were compared with

controls. In only 1 of 13 neurophysiologic indices was an abnormality found, and none of the exposed subjects were found to have a peripheral neuropathy as defined by World Health Organization criteria. These findings were confirmed in a subsequent report by the same author (29).

Similar results were reported in a study conducted 30 years after an uncontrolled chemical reaction in a trichlorophenol plant in Nitro, West Virginia, in 1949 (17). By neurological examination and nerve conduction velocity studies, no differences were found in 204 exposed subjects (55% of whom had chloracne) compared with controls. In contrast, another study of 47 railroad workers examined 6 years after exposure to polychlorinated biphenyls (PCBs), including TCDD, during a chemical spill found electrophysiologic evidence for a peripheral neuropathy in 43 of those tested by nerve conduction velocity and evoked action potential studies (30).

Point source environmental exposure to TCDD has been the focus of numerous epidemiologic studies, some of which have included neurological indices in their protocols (22-26). In 1971, waste by-products contaminated with TCDD from a chlorophenol manufacturing plant were mixed with oils and widely sprayed for dust control in residential areas of eastern Missouri. Soil concentrations in some areas reached 2,200 parts per billion. Comprehensive medical evaluations of exposed and unexposed cohorts have included detailed neurological examinations and, in one report (25), quantitative studies of tactile, vibratory, and thermal sensory perception. A recent review article summarizes the results of these Missouri dioxin studies (31). To date there has been no clinical evidence for any central or peripheral neurological disease associated with these TCDD exposures. The first study (24) to report tissue levels of dioxin in relation to neurological findings found no correlation between the body burden of dioxin and abnormalities in the peripheral indices of pain and vibratory sensation and deep tendon reflexes.

A recent report from the National Institute for Occupational Safety and Health (NIOSH) has the important strength of relating serum dioxin levels to neurological indices (21). In this study, 281 chemical plant workers were compared with 260 referents. Peripheral neuropathy was found in 18 percent of the exposed workers with serum TCDD levels ranging from 2 to 3,390 ppt (median of 68 ppt) versus a prevalence of 19 percent in referents whose TCDD levels range from 2 to 20 ppt (median of 6 ppt). There was no evidence for either a dose-response or causal relationship between TCDD and peripheral neuropathy.

Several studies of Vietnam veterans have included objective neurological data. In the Baseline examination of the Air Force Health Study (AFHS) (32), an increased incidence of abnormal Babinski reflexes was noted in Ranch Hand personnel relative to Comparisons, a finding not seen at the 1985 (33) or 1987 (34) followup examinations. Although, in the 1987 followup study, Ranch Hand participants were found to have more coordination abnormalities than Comparisons, subsequent analyses based on serum dioxin data (34) found no evidence for clinically significant neurological disease associated with the current body burden of dioxin. A few statistically significant associations were noted but not in a pattern consistent with a dose-response effect. In another study of 15 veterans who reported subjective symptoms in association with herbicide exposure, one subject was found to have a bilateral

peripheral neuropathy related to alcohol abuse. In all others, nerve conduction velocity studies at five peripheral sites were normal (35).

One large-scale study (36) of American Legion veterans who served in Vietnam found an increased incidence of reported neurobehavioral disorders among veterans thought to have been exposed to herbicides. However, the significance is limited by self-reporting bias, the lack of confirmation by clinical examination or medical record review, and the use of unvalidated exposure assumptions.

In contrast to the American Legion study, the Vietnam Experience Study (VES) conducted by the U.S. Centers for Disease Control (CDC) (37) compared 2,490 Vietnam veterans with 1,972 non-Vietnam veterans. The study protocol included comprehensive neurological examinations, nerve conduction velocity studies, and neurophysiologic indices of vibratory, thermal, and auditory sensation. Aside from an increased incidence of combat-related high-frequency hearing loss in a pattern typical of prior noise exposure, no neurological abnormalities were noted in association with service in Southeast Asia (SEA).

In summary, animal research and studies of humans exposed to high levels of dioxin leave no doubt that the peripheral nervous system is a target organ for acute TCDD toxicity. However, longitudinal studies would indicate that the neurological signs and symptoms attributable to heavy acute exposure resolve over time and are not associated with any long-term sequelae. Exposures equivalent to those likely to have been encountered by Vietnam veterans have not caused persistent neurological abnormalities.

Summary of Previous Analyses of the Air Force Health Study

1982 Baseline Study Summary Results

The 1982 AFHS neurological assessment consisted of questionnaire, physical examination, and electromyographic data obtained by examiners and technicians who were blind to the group identity of each participant. The physical examination required an average of 30 minutes to complete. Analyses were adjusted for reported alcohol usage, exposure to insecticides and industrial chemicals, and glucose intolerance (diabetes).

Results of the questionnaire disclosed no significant group differences in reported neurological diseases. The physical examination did not reveal any statistically significant group differences in the function of the 12 cranial nerves. Peripheral nerve function was assessed by the quality of four reflexes (patellar, Achilles, biceps, and Babinski); muscle strength or bulk; and reaction to the stimuli of pin prick, light touch, and vibration. Other than a statistically significant increase ($p=0.03$) in Ranch Hand Babinski reflexes, significant group differences were not detected. The alcohol covariate demonstrated a marginal effect ($p=0.07$) on pin-prick reaction, while glucose intolerance had a strong influence on the patellar and Achilles reflexes and reactions to light touch and vibration.

Nerve conduction velocities were obtained by highly standardized methods on the ulnar nerve above and below the elbow and the peroneal nerve. The results for each segmental measurement were nearly identical in the Ranch Hand and Comparison groups. Conduction

velocity showed highly significant inverse relationships to both alcohol (measured in drink-years) and glucose intolerance in almost all of the anatomic measurements. No group associations or interactions were detected with the covariates of industrial and degreasing chemicals and insecticides.

No significant group differences were detected in four measures of central neurological function (tremor, finger-nose coordination, modified positive Romberg sign, or abnormal gait). Alcohol usage was significantly associated with the presence of tremor, and glucose intolerance was highly correlated to abnormal balance and the presence of tremor.

1985 Followup Study Summary Results

The 1985 AFHS neurological examination did not include the measurements of nerve conduction velocities but otherwise repeated the Baseline examination protocol. The questionnaire maintained a historical focus on neurasthenia through five questions for the 1982-1985 interval. With this similarity in examination and questionnaire, the dependent variables of the analyses were almost identical to those of the Baseline study.

Interval questionnaire data (1982-1985) on neurological illness, verified by medical records, revealed no significant group differences. These data were added to verified Baseline historical information to assess possible differences in the lifetime experience of neurological disease. Again, there was no significant difference between the Ranch Hand and Comparison groups.

The detailed neurological examination evaluated neurological integrity in three broad areas: cranial nerve function, peripheral nerve status, and CNS coordination. Assessment of the 12 cranial nerves was based on the measurement of 15 variables. Two summary indices were constructed. Neither the unadjusted nor the adjusted analyses disclosed any statistically significant group differences, although two variables (speech and tongue position) were of marginal significance, with Ranch Hands faring worse then Comparisons. One of the two cranial nerve summary indices was marginally significant, again with the Ranch Hands at a slight detriment. In contrast to the Baseline examination, there was no significant group difference in Babinski reflex. The unadjusted and adjusted analyses of peripheral nerve function, as measured by eight variables (four reflexes, three sensory determinations, and muscle mass), did not reveal significant group differences. Coordination was evaluated by four measurements and a constructed summary variable. Hand tremor was found to be of borderline significance, with the Ranch Hands faring slightly worse than the Comparisons. The CNS summary index showed a significant detriment to the Ranch Hands.

In a longitudinal analysis of the Romberg sign and the Babinski reflex, only the Babinski reflex revealed a significant difference between the Baseline and the 1985 followup examination, with the Ranch Hands shifting from significant adverse findings at Baseline to favorable nonsignificant findings at the 1985 followup examination.

Overall, the 1985 followup examination findings are quite similar to the Baseline findings. However, several distinct patterns were evident from the analyses:

- The followup examination detected substantially fewer abnormalities for almost all measurement variables.

- The decrease in abnormalities was similar in both groups.

- The adjusted analyses were uniformly similar to the unadjusted analyses.

- A significant result was found for the constructed CNS summary variable, and a marginally significant result was found for the constructed cranial nerve index excluding range of motion.

- Although statistical significance at the pre-assigned α-level of 0.05 was not achieved for any of the measurement variables, the Ranch Hand group tended to have a greater percentage of abnormalities.

In conclusion, none of the 27 neurological variables demonstrated a significant group difference, although several showed an aggregation of abnormalities in the Ranch Hand group, which merit continued surveillance. Historical reporting of neurological disease was equal in both groups. The longitudinal analyses disclosed a favorable reversal of significant Babinski reflex abnormalities at Baseline to nonsignificant findings at the 1985 followup examination for the Ranch Hands. The similarity in results between unadjusted and adjusted statistical tests was evidence of group equality for the traditionally important neurological covariates of age, alcohol, and diabetes.

1987 Followup Study Summary Results

The neurological health of the Ranch Hand group was not substantially different from the Comparison group. Of the six questionnaire variables relating to neurological disease, the only significant finding was that Ranch Hands had a higher incidence of hereditary and degenerative neurological disease, such as benign essential tremor. The statistical results of the group contrasts for 30 physical examination variables relating to cranial nerve function, peripheral nerve status, and CNS coordination processes were generally not significant. Unadjusted analyses disclosed marginally more balance (Romberg sign) and coordination abnormalities for Ranch Hands than for Comparisons. Conversely, Ranch Hands had significantly fewer biceps reflex abnormalities than Comparisons. The longitudinal analyses for the cranial nerve index and the CNS index were not significant.

Serum Dioxin Analysis of 1987 Followup Study Summary Results

Overall, the neurological assessment did not indicate that dioxin was associated with neurological disease, although some analyses revealed a significant association with the CNS index and coordination. The adjusted analyses for the historical questionnaire variables were not significant and few statistically significant results were noted for the physical examination variables. The group contrast from the 1987 followup examination found that Ranch Hands had a significantly higher incidence of hereditary and degenerative diseases (mostly benign essential tremor) than Comparisons, but the serum dioxin analyses provided no support that dioxin levels were associated significantly with an increased risk. The adjusted categorized

current dioxin analyses for coordination found that the relative risk was significantly greater than 1 for Ranch Hands in the high current dioxin category. This is consistent with the previous report's finding that the Ranch Hand group had significantly more coordination abnormalities than the Comparison group (1.5% versus 0.6%). The serum dioxin analyses showed significant associations with the CNS index, including a marginally significant association with initial dioxin under the maximal assumption in the longitudinal analyses.

Parameters for the Neurological Assessment

Dependent Variables

The neurological assessment was based on extensive physical examination data on cranial nerve function, peripheral nerve status, and CNS coordination processes. This information was supplemented by verified histories of neurological diseases.

Medical Records Data

The 1992 questionnaire captured data on the occurrence of neurological disorders. Positive responses were verified by medical record review and combined with information from the Baseline, 1985, and 1987 examinations. The neurological diseases and disorders were classified into four ICD-9-CM categories: inflammatory diseases (ICD codes 32000-32600), hereditary and degenerative diseases (ICD codes 33000-33700), peripheral disorders (ICD codes 35000-35900), and other neurological disorders (ICD codes 34000-34900). Other neurological disorders was comprised mostly of diagnoses of unspecified encephalopathy (73.2%) but also included conditions such as multiple sclerosis, other demyelinating diseases of the central nervous system, hemiplegia, other paralytic syndromes, epilepsy, migraine, catalepsy or narcolepsy, other conditions of the brain, and other unspecified disorders of the nervous system. Each of the four disorders were coded as "yes" or "no."

Participants with positive serological tests for syphilis, participants who tested positive for the human immunosuppressant virus (HIV), and participants with a verified pre-SEA history of these disorders were excluded from all analyses of these neurological variables.

Physical Examination Data

The physical examination assessed cranial nerve function, peripheral nerve status, and CNS coordination processes. The evaluation of cranial nerve function was based on the following 14 variables: smell, visual fields, light reaction, ocular movement, facial sensation, jaw clench, smile, palpebral fissure, balance, gag reflex, speech, palate and uvula movement, neck range of motion, and the cranial nerve index excluding neck range of motion. All of these variables were scored as "normal" or "abnormal" except for jaw clench and palate and uvula movement, which were scored as "symmetric" or "deviated." For variables with left and right determinations, the two results were combined to produce a single normal or abnormal result, where normal indicated that both responses were normal, and abnormal indicated that at least one of the responses was abnormal. Abnormal speech conditions included aphasia, dysarthria, agnosia, and other abnormalities. Neck range of

motion was coded as abnormal if there was a decreased range of motion forward or backward or to the left or right. The physical examination also assessed corneal reflex and tongue position relative to midline, but these variables were not included in the analyses because there were no abnormalities.

The cranial nerve index excluding the spinal accessory nerve (nerve controlling neck range of motion) was created by combining responses for the other 12 cranial nerve parameters into a single index, which was classified as abnormal if at least one of the determinations was abnormal, and was classified as normal if all of the cranial nerve parameters were normal.

Peripheral nerve status was assessed by light pin prick, light touch (cotton sticks), visual inspection of muscle mass (and palpation, if indicated), three deep tendon reflexes (patellar, Achilles, and biceps), the Babinski reflex, and a vibrotactile measurement of both great toes using the method-of-limits (MOL) protocol (38).

Light pin prick and light touch were considered normal if the reaction was normal on both legs. A variable to appraise muscle status was constructed using data on bulk; tone of upper and lower extremities; and the strength of distal wrist extensors, ankle and toe flexors, proximal deltoids, and hip flexors. Bulk was classified as either "normal" or "abnormal"; tone was classified as "abnormal" if there was either a decreased or increased response on either the left side, right side, or both sides. The strength of distal wrist extensors, ankle and toe flexors, proximal deltoids, and hip flexors was considered abnormal if either or both the left or right side was decreased. The composite muscle status variable was classified as "normal" if all of the components were normal on both the left and right sides, and "abnormal" if any of the components was abnormal on either or both sides. The patellar, Achilles, and biceps reflexes were coded as "normal" if they were sluggish, active, or very active, and were classified as "abnormal" if absent. Participants with transient clonus or sustained clonus results were excluded from these reflex analyses.

The Vibratron II® device was used to measure vibrotactile threshold on both the left and the right great toes. The Vibratron II® provided a noninvasive means of measuring the sensitivity to vibration of a participant's feet. Participants whose great toes were able to be examined but who sensed no vibration were included in the analysis at a maximum level of 23.0 vibrational units (VU) to represent an extreme loss of sensitivity to vibration. This level of 23.0 VU is slightly higher than the highest recorded measurement in this study.

Paraplegics, amputees, and participants with other conditions not allowing testing of the great toes were not included in the analyses of the vibrotacitle threshold.

The VU measurements were transformed to displacement in microns using the following transformation:

$$Displacement\ (microns) = 0.550 \bullet VU^{2.02217}. \qquad (39)$$

The displacement measurements were transformed to the natural logarithm scale to enhance normal distribution assumptions for analysis. The left and right toes were analyzed separately. For each great toe, the average (in log microns) of four of seven trials was determined. The four trials were those remaining after eliminating the results of the first of the seven trials and the high and low reading of the other six results. A further discussion of the methodology used for analysis is given in Appendix G-1.

The evaluation of CNS coordination processes was based on the analysis of the following variables: tremor, coordination, Romberg sign, gait, and CNS index. For these variables, multiple determinations, which may have included left and right as well as upper and lower responses, were combined to form a single result. A result was classified as "normal" if all determinations were normal, and "abnormal" if any determination was abnormal. Tremor was examined for the left and right upper and lower extremities. Abnormal tremors included resting, essential, intention, and other tremors. Coordination was a composite index defined as "normal" if the Romberg sign, finger-nose-finger and heel-knee-shin coordination processes, rapidly alternating movements of pronation and supination of hands, and rapid patting were normal. The Romberg sign variable is equivalent to the balance variable analyzed as part of the cranial nerve function assessment. The gait variable was based on the examining physician's assessment of the participant's gait. An abnormal gait included conditions such as broad-based, small-stepped, ataxic or other irregular gait patterns. The CNS index was a composite variable based on tremor, coordination, and gait; this index was coded as "normal" if all three of the components were normal.

Participants with positive serological tests for syphilis and participants who tested positive for HIV were excluded from all analyses of these neurological variables. Participants with contact lenses in place were excluded from the assessment of the corneal reflex. Participants edema in the lower extremities were excluded from the analyses of pin prick and light touch.

Covariates

Age, race, military occupation, current alcohol use, lifetime alcohol history, reported exposure to insecticides, reported exposure to industrial chemicals, reported exposure to degreasing chemicals, serum insulin, and diabetic class were candidate covariates for the adjusted statistical analyses. However, based on the results of the covariate tests of association, current alcohol use, industrial chemical exposure, and serum insulin levels were not included in the adjusted analyses. Similarly, degreasing chemical exposure was not examined in the adjusted analyses for all variables except for a medical history of peripheral disorders.

The lifetime alcohol history covariate was based on self-reported information from the 1992 questionnaire, combined with information collected at the previous examinations. The respondent's average daily alcohol consumption was determined for various drinking stages throughout his lifetime, and an estimate of the corresponding total number of drink-years (1 drink-year is the equivalent of drinking 1.5 ounces of 80-proof alcoholic beverage per day

for 1 year) was derived. The current alcohol covariate was based on the average drinks per day for the month prior to completing the 1992 questionnaire.

The exposure to insecticides, industrial chemicals, and degreasing chemicals covariates represented lifetime exposure based on self-reported questionnaire data from the 1992 examination combined with data from previous examinations. Diabetic class was defined as diabetic (verified history of diabetes or $\geq$200 mg/dl 2-hour postprandial glucose), impaired (140 mg/dl $\leq$2-hour postprandial glucose$<$200 mg/dl), and normal ($<$140 mg/dl 2-hour postprandial glucose). Serum insulin levels (mIU/ml) were determined from the AFHS 1992 followup laboratory analysis. For the medical records variables, which are based on cumulative histories, lifetime alcohol history was used to investigate the cumulative effects of alcohol, and diabetic class was used to investigate the lifetime effects of diabetes on the neurological system.

Two additional variables based on self-reported information were candidate covariates for the vibrotactile measurement of both great toes: (1) a composite exposure to heavy metals, and (2) exposure to vibrating power tools. The 1992 questionnaire asked each study participant whether he had worked for 30 days or more with lead, mercury, chromium, nickel, copper, cadmium, manganese, arsenic, selenium, or molybdenum. Responses were combined to form the composite exposure to heavy metals variable. The exposure to power tools covariate was based on the 1992 questionnaire response to whether the participant had ever worked for 30 days or more with vibrating power equipment or tools.

Age and lifetime alcohol history were treated as continuous variables for all adjusted analyses, but they were categorized to explore interactions. Reported insecticides exposure, reported degreasing chemicals exposure, reported industrial chemical exposure, heavy metals exposure, and vibrating power tools exposure were categorized as "yes" or "no" for all analyses. Current alcohol use and serum insulin levels were categorized for the covariate tests of association with the discrete dependent variables, and were treated in their continuous form for the covariate tests of association with vibrotactile threshold of the left and right great toes.

Statistical Methods

Chapter 7, Statistical Methods, describes the basic statistical analysis methods used in the neurological assessment. The neurological assessment applied three modifications to the general modeling strategy delineated in Chapter 7. First, the final models for the serum dioxin analyses (Models 2 through 6) of the historical variables always retained age, regardless of statistical significance. Age always was kept in the final model because it was a potential confounder, being associated with dioxin levels and assumed to be associated with the historical conditions. Second, for models with a sparse number of abnormalities ($<$1.0%), the initial adjusted model examined main effects only, excluding interactions. The main effects included in the initial model depended on the total number of abnormalities for the variable. For example, for variables with extremely few abnormalities, age and occupation (potential confounders in the serum dioxin analyses) were the only covariates considered. A main effects model with all covariates was the starting model for variables with more abnormalities. Third, due to the large number of candidate covariates, the

covariate tests of association discussed in the Dependent Variable-Covariable Associations section were used as a preliminary screen to determine a subset of covariates to be used in the adjusted analyses.

Table 11-1 summarizes the statistical analyses performed for the 1992 neurological assessment. The first part of this table lists the dependent variables analyzed, data source, data form, cutpoints, candidate covariates, and statistical analysis methods. The second part of this table provides a description of candidate covariates examined. Abbreviations used in the body of the table are defined at the end of the table. Dependent variable and covariate data were missing for some participants. The number of participants with missing data and the number of participants excluded are provided in Table 11-2.

Analyses of data collected at the 1987 followup study indicated that dioxin was associated with military occupation. In general, enlisted personnel had higher levels of dioxin than officers, with enlisted groundcrew having higher levels than enlisted flyers. Consequently, adjustment for military occupation in statistical models using dioxin as a measure of exposure may improperly mask an actual dioxin effect. However, occupation also can be a surrogate for socioeconomic effects. Failure to adjust for occupation could overlook important risk factors related to lifestyle. If occupation was found to be significantly associated with a dependent variable in the 1992 followup analyses and was retained in the final statistical models using dioxin as a measure of exposure, the dioxin effect was evaluated in the context of two models. Analyses were performed with and without occupation in the final models to investigate whether conclusions regarding the association between the health endpoint and dioxin differed.

Diabetes also exhibited a significant positive association with dioxin in the serum dioxin analysis of the 1987 followup data. The results of similar diabetic analyses for the 1992 followup are discussed in Chapter 18, Endocrine Assessment. Consequently, clinical endpoints in the neurological assessment may be related to dioxin due to the association between dioxin and diabetes. To investigate this possibility, the dioxin effect was evaluated in the context of two models whenever diabetic class was retained in the final model. Analyses again were performed with and without diabetic class in the model to investigate whether conclusions regarding the association between the health endpoint and dioxin differed.

The results of the analyses without occupation and diabetic class in the final adjusted model are presented in Appendix G-3 and are discussed in the text only if the level of significance differs from the original final adjusted model (significant versus nonsignificant).

Longitudinal Analyses

The neurological longitudinal analyses were based on the cranial nerve index excluding neck range of motion and the CNS index. To enhance the comparability of measurements, the longitudinal assessment contrasted differences between the 1985 and 1992 Scripps Clinic and Research Facility (SCRF) neurological examinations.

Table 11-1.
Statistical Analyses for the Neurological Assessment

Dependent Variables

Variable	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Inflammatory Diseases	MR-V	D	Yes No	AGE,RACE,OCC, DRKYR,INS,IC, DC,DIAB	U:LR,CS A:LR,CS
Hereditary and Degenerative Diseases	MR-V	D	Yes No	AGE,RACE,OCC, DRKYR,INS,IC, DC,DIAB	U:LR,CS A:LR
Peripheral Disorders	MR-V	D	Yes No	AGE,RACE,OCC, DRKYR,INS,IC, DC,DIAB	U:LR,CS A:LR
Other Neurological Disorders	MR-V	D	Yes No	AGE,RACE,OCC, DRKYR,INS,IC, DC,DIAB	U:LR,CS A:LR
Smell	PE	D	Abnormal Normal	AGE,RACE,OCC,ALC, DRKYR,INS,IC,DC, INSLN,DIAB	U:LR,CS A:LR
Visual Fields	PE	D	Abnormal Normal	AGE,RACE,OCC,ALC, DRKYR,INS,IC,DC, INSLN,DIAB	U:CS A:CS
Light Reaction	PE	D	Abnormal Normal	AGE,RACE,OCC,ALC, DRKYR,INS,IC,DC, INSLN,DIAB	U:LR,CS A:LR
Ocular Movement	PE	D	Abnormal Normal	AGE,RACE,OCC,ALC, DRKYR,INS,IC,DC, INSLN,DIAB	U:LR,CS A:LR
Facial Sensation	PE	D	Abnormal Normal	AGE,RACE,OCC,ALC, DRKYR,INS,IC,DC, INSLN,DIAB	U:LR,CS, FT A:LR,CS
Jaw Clench	PE	D	Deviated Symmetric	AGE,RACE,OCC,ALC, DRKYR,INS,IC,DC, INSLN,DIAB	Frequencies
Smile	PE	D	Abnormal Normal	AGE,RACE,OCC,ALC, DRKYR,INS,IC,DC, INSLN,DIAB	U:LR,CS A:LR,CS
Palpebral Fissure	PE	D	Abnormal Normal	AGE,RACE,OCC,ALC, DRKYR,INS,IC,DC, INSLN,DIAB	U:LR,CS A:LR,CS
Balance	PE	D	Abnormal Normal	AGE,RACE,OCC,ALC, DRKYR,INS,IC,DC, INSLN,DIAB	U:LR,CS A:LR

Table 11-1. (Continued)
Statistical Analyses for the Neurological Assessment

Dependent Variables

Variable	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Gag Reflex	PE	D	Abnormal Normal	AGE,RACE,OCC,ALC, DRKYR,INS,IC,DC, INSLN,DIAB	Frequencies
Speech	PE	D	Abnormal Normal	AGE,RACE,OCC,ALC, DRKYR,INS,IC,DC, INSLN,DIAB	U:LR,CS, FT A:LR
Palate and Uvula Movement	PE	D	Deviated Symmetric	AGE,RACE,OCC,ALC, DRKYR,INS,IC,DC, INSLN,DIAB	Frequencies
Neck Range of Motion	PE	D	Abnormal Normal	AGE,RACE,OCC,ALC, DRKYR,INS,IC,DC, INSLN,DIAB	U:LR,CS A:LR
Cranial Nerve Index Without Range of Motion	PE	D	Abnormal Normal	AGE,RACE,OCC,ALC, DRKYR,INS,IC,DC, INSLN,DIAB	U:LR,CS A:LR L:LR
Pin Prick	PE	D	Abnormal Normal	AGE,RACE,OCC,ALC, DRKYR,INS,IC,DC, INSLN,DIAB	U:LR,CS A:LR
Light Touch	PE	D	Abnormal Normal	AGE,RACE,OCC,ALC, DRKYR,INS,IC,DC, INSLN,DIAB	U:LR,CS A:LR
Muscle Status	PE	D	Abnormal Normal	AGE,RACE,OCC,ALC, DRKYR,INS,IC,DC, INSLN,DIAB	U:LR,CS A:LR
Patellar Reflex	PE	D	Abnormal Normal	AGE,RACE,OCC,ALC, DRKYR,INS,IC,DC, INSLN,DIAB	U:LR,CS A:LR
Achilles Reflex	PE	D	Abnormal Normal	AGE,RACE,OCC,ALC, DRKYR,INS,IC,DC, INSLN,DIAB	U:LR,CS A:LR
Biceps Reflex	PE	D	Abnormal Normal	AGE,RACE,OCC,ALC, DRKYR,INS,IC,DC, INSLN,DIAB	U:LR,CS A:LR
Babinski Reflex	PE	D	Abnormal Normal	AGE,RACE,OCC,ALC, DRKYR,INS,IC,DC, INSLN,DIAB	U:LR,CS A:LR
Vibrotactile Threshold Measurement of Right Great Toe (microns)	PE	C	--	AGE,RACE,OCC,ALC, DRKYR,INS,IC,DC, INSLN,DIAB,HVMET, PWTOOL	U:GLM,TT A:GLM

Table 11-1. (Continued)
Statistical Analyses for the Neurological Assessment

Dependent Variables

Variable	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Vibrotactile Threshold Measurement of Left Great Toe (microns)	PE	C	--	AGE,RACE,OCC,ALC, DRKYR,INS,IC,DC, INSLN,DIAB,HVMET, PWTOOL	U:GLM,TT A:GLM
Tremor	PE	D	Abnormal Normal	AGE,RACE,OCC,ALC, DRKYR,INS,IC,DC, INSLN,DIAB	U:LR,CS A:LR
Coordination	PE	D	Abnormal Normal	AGE,RACE,OCC,ALC, DRKYR,INS,IC,DC, INSLN,DIAB	U:LR,CS A:LR
Romberg Sign	PE	D	Abnormal Normal	AGE,RACE,OCC,ALC, DRKYR,INS,IC,DC, INSLN,DIAB	U:LR,CS A:LR
Gait	PE	D	Abnormal Normal	AGE,RACE,OCC,ALC, DRKYR,INS,IC,DC, INSLN,DIAB	U:LR,CS A:LR
Central Nervous System Index	PE	D	Abnormal Normal	AGE,RACE,OCC,ALC, DRKYR,INS,IC,DC, INSLN,DIAB	U:LR,CS A:LR L:LR

Covariates

Variable (Abbreviation)	Data Source	Data Form	Cutpoints
Age (AGE)	MIL	D/C	Born $\geq$1942 Born $<$1942
Race (RACE)	MIL	D	Black Non-Black
Occupation (OCC)	MIL	D	Officer Enlisted Flyer Enlisted Groundcrew
Current Alcohol Use (ALC) (drinks/day)	Q-SR	D/C	0-1 $>$1-4 $>$4
Lifetime Alcohol History (DRKYR) (drink-years)	Q-SR	D/C	0 $>$0-40 $>$40
Insecticide Exposure (INS)	Q-SR	D	Yes No
Industrial Chemical Exposure (IC)	Q-SR	D	Yes No

Table 11-1. (Continued)
Statistical Analyses for the Neurological Assessment

Covariates

Variable (Abbreviation)	Data Source	Data Form	Cutpoints
Degreasing Chemical Exposure (DC)	Q-SR	D	Yes No
Serum Insulin (mIU/ml) (INSLN)	LAB	D/C	0-56 >56
Diabetic Class (DIAB)	LAB/MR-V	D	Diabetic: past history or ≥200 mg/dl 2-hr. postprandial glucose Impaired: ≥140-<200 mg/dl 2-hr. postprandial glucose Normal: <140 mg/dl 2-hr. postprandial glucose
Composite Exposure to Heavy Metals (HVMET)	Q-SR	D	Yes No
Worked With Vibrating Power Equipment or Tools (PWTOOL)	Q-SR	D	Yes No

Abbreviations

Data Source:
- LAB = 1992 laboratory results
- MIL = Air Force military records
- MR-V = Medical records (verified)
- PE = 1992 physical examination
- Q-SR = Health questionnaire (self-reported)

Data Form:
- C = Continuous analysis only
- D = Discrete analysis only
- D/C = Appropriate form for analysis (either discrete or continuous)

Statistical Analyses:
- U = Unadjusted analyses
- A = Adjusted analyses
- L = Longitudinal analyses

Statistical Methods:
- CS = Chi-square contingency table analysis (continuity-adjusted for 2x2 tables)
- FT = Fisher's exact test
- GLM = General linear models analysis
- LR = Logistic regression analysis
- TT = Two-sample t-test

Table 11-2.
Number of Participants with Missing Data for, or Excluded from, the Neurological Assessment

Variable	Variable Use	Group		Dioxin (Ranch Hands Only)		Categorized Dioxin	
		Ranch Hand	Comparison	Initial	Current	Ranch Hand	Comparison
Inflammatory Diseases	DEP	1	9	1	1	1	8
Hereditary and Degenerative Diseases	DEP	0	1	0	0	0	1
Peripheral Diseases	DEP	3	3	0	3	3	3
Other Neurological Disorders	DEP	4	6	1	4	4	6
Visual Fields	DEP	2	4	1	2	2	4
Light Reaction	DEP	1	2	0	1	1	2
Ocular Movement	DEP	1	2	0	1	1	2
Facial Sensation	DEP						
Corneal Reflex	DEP	8	12	3	7	7	10
Balance	DEP	1	1	1	1	1	1
Neck Range of Motion	DEP	1	0	1	1	1	0
Cranial Nerve Index Without Range of Motion	DEP	3	4	2	3	3	4
Pin Prick	DEP	0	1	0	0	0	0
Light Touch	DEP	0	1	0	0	0	0
Muscle Status	DEP	0	2	0	0	0	0
Patellar Reflex	DEP	2	4	0	2	2	3
Achilles Reflex	DEP	4	10	1	3	3	3
Babinski Reflex	DEP	0	2	0	0	0	1
Vibrotactile Threshold Measurement of Right Great Toe (microns)	DEP	2	3	2	2	2	3

Table 11-2. (Continued)
Number of Participants with Missing Data for, or Excluded from, the Neurological Assessment

Variable	Variable Use	Group		Dioxin (Ranch Hands Only)		Categorized Dioxin	
		Ranch Hand	Comparison	Initial	Current	Ranch Hand	Comparison
Vibrotactile Threshold Measurement of Left Great Toe (microns)	DEP	2	3	2	2	2	2
Coordination	DEP	1	2	1	1	1	0
Romberg Sign	DEP	1	1	1	1	1	1
Gait	DEP	0	1	0	0	0	1
Central Nervous System Index	DEP	1	1	1	1	1	0
Current Alcohol Use	COV	10	18	7	9	9	16
Lifetime Alcohol History	COV	22	21	13	20	20	18
Serum Insulin	COV	0	2	0	0	0	1
Diabetic Class	COV	1	2	0	1	1	1
Composite Exposure to Heavy Metals	COV	0	2	0	0	0	2
Worked with Vibrating Power Equipment or Tools	COV	0	2	0	0	0	2
Syphilis Positive	EXC	1	0	1	1	1	0
HIV Positive	EXC	3	1	2	3	3	1
Pre-SEA Other Neurological Disorders	EXC	4	6	1	4	4	6
Contact Lenses Not Removed	EXC	6	7	3	5	5	6
Pitting Edema on Lower Extremities	EXC	40	62	26	38	38	49

Abbreviations: DEP = Dependent variable (missing data).
COV = Covariate (missing data).
EXC = Exclusion.

Note: 952 Ranch Hands and 1,281 Comparisons;
520 Ranch Hands for initial dioxin; 894 Ranch Hands for current dioxin;
894 Ranch Hands and 1,063 Comparisons for categorized dioxin.
One Ranch Hand missing total lipids for current dioxin.

RESULTS

Dependent Variable-Covariate Associations

Covariate tests of association were performed to examine the unadjusted relationships between the covariates used in the adjusted analyses and the dependent variables. Appendix Table G-1-1 provides summary results of these analyses, presenting percents abnormal and p-values to test the statistical significance of the relationship. Statistically significant associations are discussed below.

Age

Of the four historical neurological disorder variables, age exhibited a highly significant positive association with peripheral disorders and with the category of other neurological disorders. The prevalence of peripheral disorders was higher for older participants than for younger participants ($p<0.001$, 19.4% for men born before 1942 vs. 12.2% for men born in or after 1942) as was the prevalence of other neurological disorders ($p<0.001$, 24.1% for men born before 1942 vs. 14.6% for men born in or after 1942). The covariate tests of association did not find age to be significantly associated with a history of inflammatory disease or hereditary and degenerative diseases.

Of the cranial nerve function variables analyzed at the physical examination, age showed a significant positive association with balance ($p=0.010$), neck range of motion ($p<0.001$), and the cranial nerve index (without range of motion) ($p=0.002$). The results were not significant for the other cranial nerve variables, although older participants were more likely to have abnormalities than younger participants for each variable with at least one abnormality. The nonsignificance may be partly attributable to the sparse number of abnormalities for these variables.

As expected, age was positively associated with the peripheral nerve variables of pin prick ($p=0.009$), light touch ($p=0.008$), muscle status ($p=0.009$), patellar reflex ($p<0.001$), Achilles reflex ($p<0.001$), biceps reflex ($p=0.048$), and vibrotactile threshold ($p<0.001$ for both the left and right great toes). Age also was positively associated with the central nervous system variables of coordination ($p=0.001$), Romberg sign ($p=0.010$), gait ($p=0.037$), and the CNS index ($p=0.020$).

Race

Black participants were more likely than non-Black participants to have a medical history of the category of other neurological disorders ($p<0.001$, 33.3% vs. 19.2%). Non-Blacks were more than twice as likely as Blacks to have a decreased neck range of motion ($p=0.011$, 14.6% vs. 6.2%). The only other significant association with race was that the mean vibrotactile threshold for the left great toe was significantly higher for non-Blacks than for Blacks ($p=0.019$, 16.96 microns vs. 13.23 microns).

Occupation

The covariate tests of association found a highly significant association between occupation and the category of other neurological disorders ($p<0.001$), with enlisted personnel exhibiting a higher history of disorders (26.4% of enlisted groundcrew and 30.5% of enlisted flyers) than officers (8.3%). The other neurological disorders category was comprised mostly of diagnoses of unspecified encephalopathy (416 of 568, 73.2%). There were no significant occupational differences for the other historical variables.

Neck range of motion and both left and right great toe vibrotactile threshold measurements were the only physical examination variables associated significantly with occupation ($p<0.001$ for each variable). Officers (16.8%) and enlisted flyers (17.8%) were more likely to have a decreased neck range of motion than enlisted groundcrew (10.4%). Enlisted flyers had the highest mean vibrotactile thresholds followed by officers and enlisted groundcrew.

Current Alcohol Use

Vibrotactile threshold for the left great toe was the only dependent variable significantly associated with current alcohol consumption ($p=0.017$, $r=0.051$). Because of the general nonsignificance of these results and because of the large number of candidate covariates, current alcohol consumption was not used in the adjusted analyses.

Lifetime Alcohol History

Lifetime alcohol history was associated significantly with neck range of motion ($p=0.047$), cranial nerve index (without range of motion) ($p=0.010$), vibrotactile threshold for both left and right great toes ($p<0.001$ for both great toes), tremor ($p=0.015$), and the CNS index ($p=0.030$). The percentage of neck range of motion abnormalities increased with the number of drink-years (12.7%, 12.9%, and 17.0% for men with 0 drink-years, for those with more than 0 but less than or equal to 40 drink-years, and for those with more than 40 drink-years respectively). By contrast, the highest prevalence of cranial nerve index abnormalities was seen for participants who had never drank alcohol. The prevalence rates were 9.0 percent for participants with 0 drink-years, 3.6 percent for those with between 0 and 40 drink-years and 3.7 percent for participants with more than 40 drink-years. Vibrotactile threshold levels and the percentage of tremor and central nervous system abnormalities increased with lifetime alcohol consumption.

Insecticide Exposure

The covariate tests of association found that participants who reported having been exposed to insecticides had a significantly higher prevalence of peripheral disorders than participants who had never been exposed to insecticides ($p=0.001$, 18.1% vs. 12.5%). Participants exposed to insecticides also had a significantly higher prevalence of cranial nerve index (without range of motion) abnormalities than participants who had not been exposed ($p=0.029$, 4.6% vs. 2.6%).

Industrial Chemical Exposure

A significantly higher percentage of individuals who reported being exposed to industrial chemicals had a history of other neurological disorders than individuals who had never been exposed ($p=0.001$, 22.4% vs. 16.7%). However, this association was due to the confounding effect of occupation, as enlisted personnel were more likely to have been exposed to industrial chemicals and also to have a history of other neurological diseases. An additional analysis, conducted as part of a covariate screening process to reduce the overall number of covariates, found that the association between industrial chemical exposure and other neurological disorders became nonsignificant after adjusting for occupation ($p=0.864$).

Neck range of motion and vibrotactile threshold of the right great toe also were associated significantly with industrial chemical exposure. The prevalence of decreased neck range of motion was lower for participants who had been exposed to industrial chemicals than for participants who had not been exposed ($p=0.049$, 12.8% vs. 15.9%). Participants exposed to industrial chemicals had a lower mean vibrotactile threshold in the right great toe than participants who had never been exposed ($p=0.046$, 15.96 microns vs. 17.63 microns). Both of these results also were attributable to the confounding effect of occupation and became nonsignificant after adjustment for occupation. Because of the general nonsignificance of these results and because of the large number of candidate covariates, industrial chemical exposure was not used in the adjusted analyses.

Degreasing Chemical Exposure

The covariate tests of association found that participants exposed to degreasing chemicals had a significantly higher history of peripheral disorders ($p=0.044$) and a significantly higher history of the category of other neurological disorders ($p=0.004$) than participants who had never been exposed to degreasing chemicals. Comparable to the industrial chemical exposure analyses, the association with other neurological disorders was due to the confounding effect of occupation, and became nonsignificant after adjustment for occupation ($p=0.158$). However the peripheral disorders finding remained significant even when occupation was included in the model ($p=0.014$).

Degreasing chemical exposure was not associated significantly with any of the physical examination variables. Based on these results degreasing chemical exposure was only used in the adjusted analyses of peripheral disorders.

Diabetic Class

Diabetic class was associated significantly with a history of peripheral disorders ($p<0.001$) and with a history of other neurological disorders ($p=0.001$). The percentages of individuals with peripheral disorders were 14.3 percent, 17.9 percent, and 25.6 percent for nondiabetics, glucose-impaired participants, and diabetics. The percentages of individuals with other neurological disorders were 18.1, 24.1, and 26.4 percent for nondiabetics, glucose-impaired participants, and diabetics.

Diabetic class was associated significantly with several of the cranial nerve variables including jaw clench ($p=0.020$), balance ($p<0.001$), gag reflex ($p=0.020$), palate and uvula movement ($p=0.020$), and the cranial nerve index (without range of motion) ($p=0.002$). The results for jaw clench, gag reflex, and palate and uvula movement are partly attributable to sparse data. The same individual had the only abnormality for these three variables, and he was glucose-impaired. Only frequencies are presented for these variables; no unadjusted or adjusted analyses were performed. Diabetics had the highest prevalence of balance abnormalities (2.2%) relative to impaired individuals (0.4%) and nondiabetics (0.2%). Diabetics had a higher prevalence of cranial nerve index (without range of motion) abnormalities (7.5%) than did impaired participants (2.8%) and nondiabetics (3.5%).

Diabetic class was highly associated with most of the peripheral nerve functions assessed at the neurological examination. In particular, pin prick ($p<0.001$), light touch ($p=0.001$), patellar reflex ($p<0.001$), Achilles reflex ($p<0.001$), biceps reflex ($p=0.009$), and vibrotactile threshold ($p<0.001$ for both left and right great toes) were significantly associated with diabetic class. Diabetics had relatively more peripheral reflex abnormalities and a higher mean vibrotactile threshold than impaired and normal participants. Romberg sign (identical to balance described above) was the only central nervous system variable that was associated significantly with diabetic class ($p<0.001$).

Serum Insulin

The covariate tests of association did not find a significant association between serum insulin levels and any of the neurological variables. Based on these results serum insulin was not included in the adjusted analyses.

Composite Exposure to Heavy Metals

The mean vibrotactile threshold did not differ significantly between participants exposed to heavy metals and those who had not been exposed.

Worked with Vibrating Power Equipment or Tools

Participants who had worked with vibrating power equipment or tools did not have a significantly different mean vibrotactile threshold than participants who had not worked with vibrating equipment.

Exposure Analysis

The following section presents the results of the statistical analyses of the dependent variables shown in Table 11-1. Dependent variables are grouped into two sections: those derived and verified from a review of medical records and data obtained during the 1992 physical examination.

Unadjusted and adjusted analyses of six models are presented for each variable. Model 1 examines the relationship between the dependent variable and group (Ranch Hand or Comparison). Model 2 explores the relationship between the dependent variable and an

extrapolated initial dioxin measure for Ranch Hands who had a 1987 dioxin level greater than 10 ppt. If a participant did not have a 1987 dioxin level, a 1992 level was used. A statistical adjustment for the percent of body fat at the participant's time of duty in SEA and the change in the percent body fat from the time of duty in SEA to the date of the blood draw for dioxin is included in this model to account for body-fat-related differences in elimination rate (40). Model 3 dichotomizes the Ranch Hands in Model 2 based on their initial dioxin measures; these two categories of Ranch Hands are referred to as the "low Ranch Hand" category and the "high Ranch Hand" category. These participants are added to Ranch Hands and Comparisons with current serum dioxin levels (1987, if available; 1992, if the 1987 level was not available) at or below 10 ppt to create a total of four categories. Ranch Hands with current serum dioxin levels at or below 10 ppt are referred to as the "background Ranch Hand" category. The relationship between the dependent variable in each of the three Ranch Hand categories and the dependent variable in the "Comparison" category is examined. A fourth contrast, exploring the relationship of the dependent variable in the low Ranch Hand category and the high Ranch Hand category combined, also is conducted. This combination is referred to in the text and tables as the "low plus high Ranch Hand" category. As in Model 2, a statistical adjustment is made for percent body fat at the participant's time of duty in SEA and the change in the percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

Models 4, 5, and 6 examine the relationship between the dependent variable and 1987 dioxin levels in all Ranch Hands with a dioxin measurement. If a participant did not have a 1987 dioxin measurement, a 1992 measurement was utilized in determining the current dioxin level. The measure of dioxin in Model 4 is lipid-adjusted, whereas whole-weight dioxin is used in Models 5 and 6. Model 6 differs from Model 5 in that a statistical adjustment for total lipids is included in Model 6. Further details on dioxin and the modeling strategy are found in Chapters 2 and 7 respectively.

Results of investigations for group-by-covariate and dioxin-by-covariate interactions are referenced in the text, and tabular results are presented in Appendix G-2. As described previously, additional analyses were performed when occupation or body fat was retained in the final model for Models 2 through 6. Results excluding occupation and body fat from these models are tabled in Appendix G-3, and dioxin-by-covariate interactions with occupation and body fat excluded from these models are presented in Appendix G-4. Results from analyses excluding occupation and body fat are discussed in the text only if a meaningful change in the results occurred (that is, changes between significant results, marginally significant results, and nonsignificant results).

Medical Records Variables: Historical Neurological Disorders

Inflammatory Diseases

The unadjusted Model 1 analyses showed that the percentage of participants with a history of inflammatory disease did not differ significantly between the Ranch Hand and Comparison groups, although the estimated relative risk was more than four (Table 11-3(a): $p=0.136$, Est. RR: 4.05, 95% C.I.=[0.82, 20.09]). There were eight participants with a history of inflammatory disease, six Ranch Hands and two Comparisons. Within each of the

occupational cohorts, Ranch Hands had a higher prevalence of inflammatory diseases than Comparisons, although these differences were not significant ($p > 0.38$ within each stratum). The adjusted Model 1 analyses were identical to the unadjusted analysis because no covariates were retained in the final model.

For Model 2, the unadjusted and adjusted analyses did not show a significant association between initial dioxin and inflammatory disease (Table 11-3(c,d): $p > 0.70$ for both analyses). The adjusted model contained the covariate age.

The unadjusted and adjusted Model 3 analyses did not reveal a significant contrast involving the Comparison group (Table 11-3(e,f): $p > 0.10$ for all contrasts) although a dose-response pattern was seen and the adjusted relative risk was nearly five for the high dioxin category (Table 11-3(f): $p=0.133$, Adj. RR=4.72, 95% C.I.=[0.62, 35.64]). The adjusted analysis included the covariate age. The percentages of participants with a history of inflammatory disease were 0.2 for the Comparison group and 0.3, 0.4, and 0.8 for Ranch Hands in the background, low, and high dioxin categories respectively.

Presented in Table 11-3(g,h), the unadjusted and adjusted results for Models 4 through 6 did not reveal a significant association between current dioxin and inflammatory disease ($p > 0.52$ for all analyses). Each of the adjusted analyses contained the covariate age.

Hereditary and Degenerative Diseases

The unadjusted and adjusted Model 1 analyses did not reveal a significant group difference in the percentage of participants with hereditary and degenerative diseases (Table 11-4(a,b): $p > 0.35$ for all contrasts). Age was retained in the final adjusted model.

The unadjusted Model 2 analysis did not reveal a significant association between initial dioxin and hereditary and degenerative diseases (Table 11-4(c): $p=0.712$). The initial dioxin-by-occupation interaction was significant in the adjusted analysis of Model 2 (Table 11-4(d): $p=0.028$). Appendix Table G-2-1 displays adjusted results stratified by occupation. In addition to the initial dioxin-by-occupation interaction, the adjusted analysis contained age and the lifetime alcohol history-by-insecticide interaction. The adjusted analysis did not detect a significant association between initial dioxin and hereditary diseases when the initial dioxin-by-occupation interaction was removed from the final model (Table 11-4(d): $p=0.379$).

For Model 3, the unadjusted and adjusted analyses did not show any of the Ranch Hand categories to be significantly different from the Comparison group in the percentages of participants with hereditary and degenerative diseases (Table 11-4(e,f): $p \geq 0.42$ for all contrasts). The final adjusted model included age, occupation, and lifetime alcohol history.

The unadjusted analyses for Models 4 and 5 did not find a significant association between current dioxin and hereditary and degenerative diseases (Table 11-4(g): $p > 0.14$ for both analyses). However, the unadjusted Model 6 analysis revealed a marginally significant inverse association between current dioxin and hereditary and degenerative diseases (Table 11-4(g): $p=0.096$, Est. RR=0.86, 95% C.I.=[0.72,1.03]).

Table 11-3.
Analysis of Inflammatory Diseases

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***947***	***0.6***	***4.05 (0.82,20.09)***	***0.136***
	Comparison	***1,271***	***0.2***		
Officer	Ranch Hand	367	0.5	2.72 (0.25,30.09)	0.792
	Comparison	497	0.2		
Enlisted Flyer	Ranch Hand	162	1.2	--	0.388
	Comparison	200	0.0		
Enlisted Groundcrew	Ranch Hand	418	0.5	2.76 (0.25,30.48)	0.782
	Comparison	574	0.2		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks**
All	***4.05 (0.82,20.09)***	***0.136***	
Officer	2.72 (0.25,30.09)	0.792	
Enlisted Flyer	--	0.388	
Enlisted Groundcrew	2.76 (0.25,30.48)	0.782	

--: Relative risk and confidence interval not presented due to the sparse number of abnormalities.

Table 11-3. (Continued)
Analysis of Inflammatory Diseases

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent Yes**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	174	0.0	1.09 (0.51,2.35)	0.826
Medium	173	0.6		
High	169	1.2		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
	Analysis Results for Log_2 (Initial Dioxin)[c]		
n	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**	**Covariate Remarks**
516	0.85 (0.35,2.03)	0.705	AGE (p=0.165)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 11-3. (Continued)
Analysis of Inflammatory Diseases

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,054	0.2		
Background RH	373	0.3	1.14 (0.10,12.72)	0.916
Low RH	260	0.4	2.19 (0.20,24.61)	0.525
High RH	256	0.8	5.14 (0.70,37.90)	0.108
Low plus High RH	516	0.6	3.53 (0.57,21.74)	0.174

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,054			AGE (p=0.539)
Background RH	373	1.19 (0.11,13.33)	0.889	
Low RH	260	2.23 (0.20,24.93)	0.516	
High RH	256	4.72 (0.62,35.64)	0.133	
Low plus High RH	516	3.39 (0.55,20.96)	0.188	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 11-3. (Continued)
Analysis of Inflammatory Diseases

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Yes/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	0.3 (294)	0.3 (300)	0.7 (295)	1.20 (0.63,2.27)	0.586
5	0.3 (299)	0.3 (297)	0.7 (293)	1.14 (0.64,2.03)	0.654
6[c]	0.3 (298)	0.3 (297)	0.7 (293)	1.23 (0.66,2.27)	0.521

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	n	Analysis Results for Log_2 (Current Dioxin + 1) Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	889	1.10 (0.57,2.10)	0.781	AGE (p=0.321)
5	889	1.06 (0.60,1.88)	0.833	AGE (p=0.306)
6[d]	888	1.13 (0.61,2.09)	0.706	AGE (p=0.347)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 11-4.
Analysis of Hereditary and Degenerative Diseases

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***948***	***5.6***	***1.09 (0.75,1.58)***	***0.725***
	Comparison	***1,279***	***5.2***		
Officer	Ranch Hand	367	4.9	1.07 (0.57,2.01)	0.963
	Comparison	500	4.6		
Enlisted Flyer	Ranch Hand	162	5.6	0.74 (0.31,1.73)	0.624
	Comparison	203	7.4		
Enlisted Groundcrew	Ranch Hand	419	6.2	1.30 (0.75,2.24)	0.434
	Comparison	576	4.9		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	***1.08 (0.75,1.57)***	***0.683***	AGE (p=0.009)
Officer	1.06 (0.56,1.99)	0.861	
Enlisted Flyer	0.73 (0.31,1.71)	0.465	
Enlisted Groundcrew	1.30 (0.75,2.25)	0.356	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 11-4. (Continued)
Analysis of Hereditary and Degenerative Diseases

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	174	6.9	0.95 (0.70,1.28)	0.712
Medium	173	4.0		
High	170	5.3		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
504	0.85 (0.59,1.22)**	0.379**	INIT*OCC (p=0.028) AGE (p=0.168) DRKYR*INS (p=0.021)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table G-2-1 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
INIT = Log_2 (initial dioxin).

Table 11-4. (Continued)
Analysis of Hereditary and Degenerative Diseases

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,061	5.6		
Background RH	373	6.4	1.10 (0.67,1.80)	0.714
Low RH	260	5.8	1.09 (0.61,1.95)	0.778
High RH	257	5.1	0.94 (0.51,1.75)	0.846
Low plus High RH	517	5.4	1.01 (0.64,1.62)	0.952

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,043			AGE (p=0.003) OCC (p=0.120) DRKYR (p=0.137)
Background RH	366	1.19 (0.72,1.99)	0.498	
Low RH	254	1.00 (0.55,1.83)	0.997	
High RH	250	0.76 (0.38,1.49)	0.420	
Low plus High RH	504	0.88 (0.54,1.44)	0.606	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 11-4. (Continued)
Analysis of Hereditary and Degenerative Diseases

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Yes/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	7.5 (294)	5.0 (300)	5.1 (296)	0.86 (0.70,1.06)	0.145
5	7.0 (299)	5.1 (297)	5.4 (294)	0.89 (0.75,1.04)	0.148
6[c]	7.0 (298)	5.1 (297)	5.4 (294)	0.86 (0.72,1.03)	0.096

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	889	0.79 (0.63,0.98)	0.030	AGE (p=0.923) OCC*DIAB (p=0.027)
5	889	0.83 (0.70,0.98)	0.033	AGE (p=0.898) OCC*DIAB (p=0.026)
6[d]	868	0.76 (0.62,0.93)	0.009	AGE (p=0.390) OCC*DRKYR (p=0.003) DIAB*DRKYR (p=0.003) OCC*DIAB (p=0.005)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

The adjusted results for Models 4 through 6 differed from the unadjusted results in that each of the adjusted analyses revealed a significant inverse association between current dioxin and hereditary and degenerative diseases (Table 11-4(h): $p=0.030$, Adj. RR=0.79, 95% C.I.=[0.63,0.98] for Model 4; $p=0.033$, Adj. RR=0.83, 95% C.I.=[0.70,0.98] for Model 5; and $p=0.009$, Adj. RR=0.76, 95% C.I.=[0.62,0.93] for Model 6). The adjusted analyses for Models 4 and 5 contained the covariate age and the occupation-by-diabetic class interaction. The Model 6 adjusted analysis included the covariate age and three covariate-by-covariate interactions: occupation-by-lifetime alcohol history, diabetic class-by-lifetime alcohol history, and occupation-by-diabetic class.

Without occupation and diabetic class, the adjusted results resembled the unadjusted results. The analyses for Models 4 and 5 did not find a significant association between current dioxin and hereditary and degenerative diseases (Appendix Table G-3-1(c): $p>0.16$ for both analyses); however, the Model 6 analysis revealed a marginally significant inverse association between current dioxin and hereditary and degenerative diseases (Appendix Table G-3-1(c): $p=0.069$, Adj. RR=0.84, 95% C.I.=[0.70,1.01]).

Peripheral Disorders

The unadjusted and adjusted Model 1 analyses did not reveal a significant group difference in the percentage of peripheral disorders (Table 11-5(a,b): $p>0.34$ for all contrasts). The adjusted analysis contained the covariates diabetic class, insecticide exposure, and degreasing chemical exposure, and an age-by-occupation interaction.

In Model 2, the unadjusted and adjusted analyses did not reveal a significant association between initial dioxin and peripheral disorders (Table 11-5(c,d): $p>0.53$ for both analyses). The final adjusted model contained the covariates age, race, and diabetic class.

The unadjusted and adjusted analyses for Model 3 did not reveal a significant difference between any of the Ranch Hand categories and the Comparison group (Table 11-5(e,f): $p>0.47$ for all contrasts). The adjusted analysis included diabetic class, degreasing chemical exposure, and two covariate-by-covariate interactions: age-by-occupation and age-by-insecticide exposure.

The unadjusted results for Models 4 through 6 did not reveal a significant association between current dioxin and peripheral disorders (Table 11-5(g): $p>0.25$ for all analyses). Each of the adjusted analyses for Models 4 through 6 contained a significant interaction between current dioxin and lifetime alcohol history (Table 11-5(h): $p=0.017$, $p=0.025$, and $p=0.040$ for Models 4, 5, and 6 respectively). Appendix Table G-2-2 presents adjusted results stratified by lifetime alcohol history for Models 4 through 6. In addition to the current dioxin-by-lifetime alcohol history interaction, each of the adjusted analyses included race, diabetic class, insecticide exposure, and an age-by-occupation interaction. Without the current dioxin-by-lifetime alcohol history interaction, none of the adjusted analyses for Models 4 through 6 detected a significant association between current dioxin and peripheral disorders (Table 11-5(h): $p>0.20$ for all analyses).

Table 11-5.
Analysis of Peripheral Disorders

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***945***	***16.9***	***1.08 (0.86,1.35)***	***0.552***
	Comparison	***1,277***	***15.9***		
Officer	Ranch Hand	366	18.3	1.21 (0.85,1.73)	0.343
	Comparison	499	15.6		
Enlisted Flyer	Ranch Hand	161	18.0	1.05 (0.61,1.80)	0.975
	Comparison	202	17.3		
Enlisted Groundcrew	Ranch Hand	418	15.3	0.98 (0.69,1.38)	0.963
	Comparison	576	15.6		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	***1.01 (0.80,1.28)***	***0.923***	DIAB (p=0.002)
Officer	1.15 (0.79,1.67)	0.455	INS (p=0.006)
Enlisted Flyer	0.95 (0.55,1.64)	0.850	DC (p=0.033)
Enlisted Groundcrew	0.92 (0.65,1.32)	0.663	AGE*OCC (p=0.015)

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 11-5. (Continued)
Analysis of Peripheral Disorders

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent Yes**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	174	17.8	1.04 (0.88,1.23)	0.673
Medium	173	17.9		
High	170	18.8		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
	Analysis Results for Log_2 (Initial Dioxin)[c]		
n	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**	**Covariate Remarks**
517	1.06 (0.88,1.27)	0.531	AGE (p=0.288) RACE (p=0.072) DIAB (p=0.009)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 11-5. (Continued)
Analysis of Peripheral Disorders

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,059	16.7		
Background RH	370	16.2	0.99 (0.72,1.37)	0.947
Low RH	260	18.8	1.14 (0.80,1.62)	0.472
High RH	257	17.5	1.04 (0.72,1.49)	0.837
Low plus High RH	517	18.2	1.09 (0.82,1.44)	0.550

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,058			DIAB ($p<0.001$) DC ($p=0.086$) AGE*OCC ($p=0.001$) AGE*INS ($p=0.035$)
Background RH	369	0.93 (0.66,1.30)	0.662	
Low RH	260	0.97 (0.68,1.40)	0.881	
High RH	257	1.04 (0.71,1.53)	0.824	
Low plus High RH	517	1.01 (0.75,1.34)	0.971	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$ 10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin $\leq$ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 11-5. (Continued)
Analysis of Peripheral Disorders

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Yes/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	13.0 (292)	21.1 (299)	17.9 (296)	1.07 (0.95,1.21)	0.253
5	13.5 (296)	19.9 (297)	18.7 (294)	1.06 (0.95,1.17)	0.294
6[c]	13.5 (296)	19.9 (297)	18.7 (294)	1.06 (0.95,1.19)	0.286

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	n	Analysis Results for Log_2 (Current Dioxin + 1) Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	866	1.10 (0.95,1.28)**	0.204**	CURR*DRKYR (p=0.017) RACE (p=0.120) DIAB (p=0.045) INS (p=0.041) AGE*OCC (p=0.001)
5	866	1.07 (0.94,1.21)**	0.311**	CURR*DRKYR (p=0.025) RACE (p=0.120) DIAB (p=0.049) INS (p=0.040) AGE*OCC (p<0.001)
6[d]	866	1.09 (0.95,1.25)**	0.202**	CURR*DRKYR (p=0.040) RACE (p=0.110) DIAB (p=0.040) INS (p=0.040) AGE*OCC (p<0.001)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table G-2-2 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.
CURR = Log_2 (current dioxin + 1).

The adjusted results for Models 4 through 6 changed substantially when occupation and diabetic class were removed from each of the final models. Without these covariates and without the current dioxin-by-lifetime alcohol history interaction, each of the adjusted models detected a significant positive association between current dioxin and peripheral disorders (Appendix Table G-3-2(c): $p=0.024$, Adj. RR=1.16, 95% C.I.=[1.02,1.31]; $p=0.043$, Adj. RR=1.12, 95% C.I.=[1.00,1.25]; and $p=0.027$, Adj. RR=1.14, 95% C.I.=[1.01,1.29] for Models 4, 5, and 6 respectively).

Other Neurological Disorders

The unadjusted and adjusted Model 1 analyses did not find a significant group difference in the percentage of participants with other neurological disorders (Table 11-6(a,b): $p>0.22$ for all contrasts). The final adjusted model contained the covariates age, race, and occupation.

For Model 2, the unadjusted and adjusted analyses did not reveal a significant association between initial dioxin and other neurological disorders (Table 11-6(c,d): $p>0.32$ for both analyses). Age and occupation were retained in the adjusted analysis. When occupation was removed from the final model, a significant positive association was found between other neurological disorders and initial dioxin (Appendix Table G-3-3(a): $p=0.022$, Adj. RR=1.21, 95% C.I.=[1.03,1.42]).

The unadjusted Model 3 analysis of other neurological disorders found a significant difference between the high Ranch Hands and Comparisons: (Table 11-6(e): $p=0.040$, Est. RR=1.40, 95% C.I.=[1.01,1.92]). The percentage of other neurological disorders was higher for the high Ranch Hands than for the Comparisons (26.1% versus 20.4%). The low plus high Ranch Hand versus Comparison contrast was marginally significant ($p=0.055$), Adj. RR=1.28, 95% C.I.=[0.99,1.65]). After adjusting for age, race, and occupation, the adjusted analysis did not show any of the Ranch Hands categories to be significantly different from the Comparison group (Table 11-6(f): $p>0.50$ for all contrasts).

The adjusted results changed when occupation was removed from the final model. Without occupation, the adjusted analysis detected a marginally significant difference for the background Ranch Hands, and a significant difference for the high Ranch Hands and the low plus high Ranch Hands. The adjusted relative risk was less than 1.00 for the background Ranch Hands and greater than 1.00 for the high Ranch Hands and the low plus high Ranch Hands (Appendix Table G-3-3(b): $p=0.061$, Adj. RR=0.74, 95% C.I.=[0.53,1.01]; $p=0.002$, Adj. RR=1.69, 95% C.I.=[1.21,2.36]; and $p=0.034$, Adj. RR=1.32, 95% C.I.=[1.02,1.71] for the background Ranch Hands, high Ranch Hands, and low plus high Ranch Hands respectively).

The unadjusted analyses for Models 4 and 6 detected a significant positive association between current dioxin and other neurological disorders (Table 11-6(g): $p=0.022$, Est. RR=1.14, 95% C.I.=[1.02,1.27] and $p=0.011$, Est. RR=1.14, 95% C.I.=[1.03,1.27] for Models 4 and 6 respectively). For Model 5, the unadjusted analysis revealed a marginally significant association between current dioxin and other neurological disorders (Table 11-6(g): $p=0.070$, Est. RR=1.09, 95% C.I.=[0.99,1.20]).

Table 11-6.
Analysis of Other Neurological Disorders

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***944***	***21.2***	***1.14 (0.92,1.40)***	***0.258***
	Comparison	***1,274***	***19.2***		
Officer	Ranch Hand	365	8.5	1.04 (0.64,1.69)	0.976
	Comparison	500	8.2		
Enlisted Flyer	Ranch Hand	162	31.5	1.09 (0.70,1.70)	0.801
	Comparison	202	29.7		
Enlisted Groundcrew	Ranch Hand	417	28.3	1.18 (0.89,1.57)	0.276
	Comparison	572	25.0		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.14 (0.91,1.43)***	***0.269***	AGE ($p<0.001$) RACE ($p=0.011$) OCC ($p<0.001$)
Officer	1.04 (0.63,1.70)	0.891	
Enlisted Flyer	1.07 (0.67,1.70)	0.779	
Enlisted Groundcrew	1.21 (0.89,1.63)	0.223	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 11-6. (Continued)
Analysis of Other Neurological Disorders

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent Yes**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	174	21.3	1.08 (0.93,1.25)	0.323
Medium	172	27.3		
High	170	25.9		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**	**Covariate Remarks**
516	0.96 (0.80,1.15)	0.649	AGE ($p<0.001$) OCC ($p<0.001$)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 11-6. (Continued)
Analysis of Other Neurological Disorders

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,056	20.4		
Background RH	370	16.8	0.79 (0.57,1.08)	0.132
Low RH	259	23.6	1.17 (0.85,1.62)	0.339
High RH	257	26.1	1.40 (1.01,1.92)	0.040
Low plus High RH	516	24.8	1.28 (0.99,1.65)	0.055

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,056			AGE ($p<0.001$) RACE ($p=0.002$) OCC ($p<0.001$)
Background RH	370	1.13 (0.79,1.60)	0.506	
Low RH	259	1.09 (0.76,1.55)	0.649	
High RH	257	1.02 (0.72,1.45)	0.902	
Low plus High RH	516	1.05 (0.80,1.38)	0.714	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 11-6. (Continued)
Analysis of Other Neurological Disorders

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Yes/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	16.1 (292)	20.7 (299)	27.5 (295)	1.14 (1.02,1.27)	0.022
5	16.5 (297)	23.3 (296)	24.6 (293)	1.09 (0.99,1.20)	0.070
6[c]	16.2 (296)	23.3 (296)	24.6 (293)	1.14 (1.03,1.27)	0.011

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	886	0.96 (0.84,1.09)	0.547	AGE ($p<0.001$) RACE ($p=0.009$) OCC ($p<0.001$)
5	886	0.94 (0.84,1.05)	0.268	AGE ($p<0.001$) RACE ($p=0.010$) OCC ($p<0.001$)
6[d]	885	0.99 (0.88,1.11)	0.834	AGE ($p<0.001$) RACE ($p=0.015$) OCC ($p<0.001$)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

By contrast, the adjusted analyses for Models 4 through 6 did not show a significant association between current dioxin and other neurological disorders (Table 11-6(h): $p > 0.26$ for all analyses). Each of the adjusted analyses for Models 4 through 6 contained the covariates age, race, and occupation.

The adjusted results changed after occupation was removed from each of the final models. Without occupation in the models, each of the adjusted analyses for Models 4 through 6 revealed a significant association between current dioxin and other neurological disorders (Appendix Table G-3-3(c): $p < 0.001$, Adj. RR=1.24, 95% C.I.=[1.10,1.39]; $p=0.003$, Adj. RR=1.17, 95% C.I.=[1.05,1.29]; and $p=0.001$, Adj. RR=1.24, 95% C.I.=[1.11,1.39] for Models 4, 5, and 6 respectively).

Physical Examination Variables: Cranial Nerve Function

Smell

The unadjusted and adjusted Model 1 analyses of smell did not find a significant group difference in the percentage of smell abnormalities (Table 11-7(a,b): $p > 0.26$ for all contrasts). The covariate age was included in the final adjusted model.

The unadjusted results for Model 2 did not reveal a significant association between initial dioxin and smell (Table 11-7(c): $p=0.341$). Because no covariates were retained in the final model, the unadjusted and adjusted results were the same.

For Model 3, the unadjusted analysis of smell did not show any of the Ranch Hand categories to be significantly different from the Comparison group (Table 11-7(e): $p > 0.22$ for all contrasts). The adjusted Model 3 analysis contained a significant interaction between categorized dioxin and insecticide exposure (Table 11-7(f): $p=0.006$). Appendix Table G-2-3 displays adjusted results stratified by insecticide exposure. The adjusted analysis also included the covariate age. Without the categorized dioxin-by-insecticide exposure, the adjusted analysis did not reveal any significant contrasts involving the Comparison group (Table 11-7(f): $p > 0.25$ for all contrasts).

The unadjusted analyses for Models 4 through 6 revealed a significant inverse association between current dioxin and smell (Table 11-7(g): $p=0.018$, Est. RR=0.61, 95% C.I.=[0.39,0.93]; $p=0.015$, Est. RR=0.69, 95% C.I.=[0.52,0.91]; and $p=0.019$, Est. RR=0.68, 95% C.I.=[0.50,0.92] for Models 4, 5, and 6 respectively). None of the adjusted analyses for Models 4, 5, and 6 retained any covariates; therefore, the adjusted results were identical to the unadjusted results for each of these models.

Visual Fields

The unadjusted Model 1 analysis did not detect a significant group difference in the percentage of visual field abnormalities (Table 11-8(a): $p > 0.61$ for all contrasts). No covariates were retained in the final model; therefore, the adjusted and unadjusted results were identical.

Table 11-7.
Analysis of Smell

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***948***	***1.5***	***1.11 (0.55,2.27)***	***0.910***
	Comparison	***1,280***	***1.3***		
Officer	Ranch Hand	367	1.1	0.60 (0.18,1.97)	0.573
	Comparison	501	1.8		
Enlisted Flyer	Ranch Hand	162	1.9	1.26 (0.25,6.32)	0.999
	Comparison	203	1.5		
Enlisted Groundcrew	Ranch Hand	419	1.7	1.94 (0.61,6.16)	0.395
	Comparison	576	0.9		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.10 (0.54,2.25)***	***0.790***	AGE (p=0.017)
Officer	0.59 (0.18,1.95)	0.391	
Enlisted Flyer	1.24 (0.25,6.22)	0.797	
Enlisted Groundcrew	1.94 (0.61,6.16)	0.262	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 11-7. (Continued)
Analysis of Smell

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent Abnormal**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	174	1.7	0.69 (0.31,1.55)	0.341
Medium	173	0.6		
High	170	0.6		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[a]			
n	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**	**Covariate Remarks**
517	0.69 (0.31,1.55)	0.341	

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 11-7. (Continued)
Analysis of Smell

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,062	1.3		
Background RH	373	2.1	1.70 (0.70,4.12)	0.243
Low RH	260	1.5	1.15 (0.37,3.53)	0.807
High RH	257	0.4	0.28 (0.04,2.18)	0.227
Low plus High RH	517	1.0	0.72 (0.26,2.01)	0.526

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,062			DXCAT*INS (p=0.006) AGE (p=0.082)
Background RH	373	1.49 (0.61,3.65)**	0.379**	
Low RH	260	1.00 (0.32,3.09)**	0.996**	
High RH	257	0.31 (0.04,2.37)**	0.257**	
Low plus High RH	517	0.69 (0.24,1.95)**	0.482**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table G-2-3 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.
DXCAT = Categorized Dioxin.

Table 11-7. (Continued)
Analysis of Smell

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	2.4 (294)	1.7 (300)	0.3 (296)	0.61 (0.39,0.93)	0.018
5	2.3 (299)	1.7 (297)	0.3 (294)	0.69 (0.52,0.91)	0.015
6[c]	2.3 (298)	1.7 (297)	0.3 (294)	0.68 (0.50,0.92)	0.019

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	890	0.61 (0.39,0.93)	0.018	
5	890	0.69 (0.52,0.91)	0.015	
6[c]	889	0.68 (0.50,0.92)	0.019	

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 11-8.
Analysis of Visual Fields

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***946***	***0.1***	***0.45 (0.05,4.32)***	***0.837***
	Comparison	***1,276***	***0.2***		
Officer	Ranch Hand	367	0.0	--	0.619
	Comparison	500	0.4		
Enlisted Flyer	Ranch Hand	162	0.0	--	--
	Comparison	203	0.0		
Enlisted Groundcrew	Ranch Hand	417	0.2	1.38 (0.09,22.05)	0.999
	Comparison	573	0.2		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
All	***0.45 (0.05,4.32)***	***0.837***	
Officer	--	0.619	
Enlisted Flyer	--	--	
Enlisted Groundcrew	1.38 (0.09,22.05)	0.999	

--: Relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

Table 11-8. (Continued)
Analysis of Visual Fields

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)**	
Initial Dioxin	**n**	**Percent Abnormal**	**Estimated Relative Risk (95% C.I.)**	**p-Value**
Low	174	0.0	--	--
Medium	173	0.0		
High	169	0.0		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)			
n	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks**
--	--	--	

--: Analysis not conducted due to the sparse number of abnormalities.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 11-8. (Continued)
Analysis of Visual Fields

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)	p-Value
Comparison	1,058	0.1		
Background RH	372	0.3	--	--
Low RH	260	0.0	--	--
High RH	256	0.0	--	--
Low plus High RH	516	0.0	--	--

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Comparison	--			
Background RH	--	--	--	
Low RH	--	--	--	
High RH	--	--	--	
Low plus High RH	--	--	--	

--: Analysis not conducted due to the sparse number of abnormalities.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 11-8. (Continued)
Analysis of Visual Fields

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)	p-Value
4	0.3 (293)	0.0 (300)	0.0 (295)	--	--
5	0.3 (298)	0.0 (297)	0.0 (293)	--	--
6	0.3 (297)	0.0 (297)	0.0 (293)	--	--

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
4	--	--	--	
5	--	--	--	
6	--	--	--	

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

--: Analysis not conducted due to the sparse number of abnormalities.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Statistical analyses were not conducted for Models 2 through 6 due to the sparse number of abnormalities. There were no abnormalities in the Model 2 analysis. For Model 3, the background Ranch Hand category and Comparison group each contained one abnormality. There were no abnormalities in the low Ranch Hand and high Ranch Hand categories. Each of the analyses for Models 4 through 6 included only one abnormal participant. The participant in each analysis was in the low current dioxin category. Table 11-8(c,e,g) presents frequencies and percentages of abnormalities for these models.

Light Reaction

The unadjusted Model 1 analysis did not reveal a significant overall group difference in the percentage of light reaction abnormalities (Table 11-9(a): $p=0.433$). However, stratifying the unadjusted analysis by occupation revealed a marginally significant group difference within the enlisted groundcrew stratum (Table 11-9(a): $p=0.066$). Of the enlisted groundcrew, four Ranch Hands had light reaction abnormalities whereas none of the enlisted groundcrew Comparisons displayed light reaction abnormalities.

The adjusted Model 1 analysis did not show the percentage of light reaction abnormalities to be significantly different between the Ranch Hands and Comparisons (Table 11-9(b): $p>0.255$ for all contrasts). For the enlisted groundcrew, a relative risk and p-value were not calculated because no Comparisons experienced an abnormal light reaction. The final adjusted model contained diabetic class.

The unadjusted Model 2 results did not reveal a significant association between initial dioxin and light reaction even though the estimated relative risk was 1.43 for a twofold increase in initial dioxin (Table 11-9(c): $p=0.384$). Only four individuals in the Model 2 analysis displayed light reaction abnormalities. Two of those four participants had a high initial dioxin level. The adjusted results for Model 2 were identical to the unadjusted findings because no covariates were retained in the final model.

The unadjusted Model 3 analysis of light reaction abnormalities revealed a marginally significant difference between the low plus high Ranch Hand category and the Comparisons group (Table 11-9(e): $p=0.061$, Est. RR=5.18, 95% C.I.=[0.93,28.94]. The percentages of abnormalities for the low plus high Ranch Hand category and the Comparison group were 0.8 percent and 0.2 percent respectively. The estimated relative risks for the low Ranch Hands and the high Ranch Hands exceeded five but were not significant (Table 11-9(e): $p>0.10$ for both contrasts). The adjusted and unadjusted results were identical because no covariates were retained in the final model.

The unadjusted analyses for Models 4 through 6 did not reveal a significant association between current dioxin and light reaction even though each of the estimated relative risks for a twofold increase in current dioxin was greater than or equal to 1.30 (Table 11-9(g): $p>0.22$ for all analyses). Only five participants displayed abnormal light reactions in the analyses of Models 4 through 6. Three of the five abnormal participants had a high current dioxin level in each of the models. For Models 4 through 6, the adjusted analysis did not differ from the unadjusted analysis because no covariates were retained in the final model.

Table 11-9.
Analysis of Light Reaction

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***947***	***0.5***	***2.26 (0.54,9,47)***	***0.433***
	Comparison	***1,278***	***0.2***		
Officer	Ranch Hand	367	0.3	0.68 (0.06,7.54)	0.999
	Comparison	501	0.4		
Enlisted Flyer	Ranch Hand	162	0.0	--	0.999
	Comparison	203	0.5		
Enlisted Groundcrew	Ranch Hand	418	1.0	--	0.066
	Comparison	574	0.0		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***2.27 (0.54,9.50)***	***0.255***	DIAB (p=0.140)
Officer	0.64 (0.06,7.14)	0.720	
Enlisted Flyer	--	--	
Enlisted Groundcrew	--	--	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

--: Relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

Table 11-9. (Continued)
Analysis of Light Reaction

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	174	0.6	1.43 (0.64,3.20)	0.384
Medium	173	0.6		
High	170	1.2		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[a]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
517	1.43 (0.64,3.20)	0.384	

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 11-9. (Continued)
Analysis of Light Reaction

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,060	0.2		
Background RH	372	0.3	1.07 (0.10,11.97)	0.956
Low RH	260	0.8	5.05 (0.70,36.61)	0.109
High RH	257	0.8	5.31 (0.72,39.12)	0.101
Low plus High RH	517	0.8	5.18 (0.93,28.94)	0.061

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ab]	p-Value	Covariate Remarks
Comparison	1,060			
Background RH	372	1.07 (0.10,11.97)	0.956	
Low RH	260	5.05 (0.70,36.61)	0.109	
High RH	257	5.31 (0.72,39.12)	0.101	
Low plus High RH	517	5.18 (0.93,28.94)	0.061	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 11-9. (Continued)
Analysis of Light Reaction

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	0.3 (293)	0.3 (300)	1.0 (296)	1.38 (0.80,2.39)	0.260
5	0.3 (298)	0.3 (297)	1.0 (294)	1.37 (0.83,2.26)	0.221
6[c]	0.3 (297)	0.3 (297)	1.0 (294)	1.30 (0.76,2.23)	0.346

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	889	1.38 (0.80,2.39)	0.260	
5	889	1.37 (0.83,2.26)	0.221	
6[c]	888	1.30 (0.76,2.23)	0.346	

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Ocular Movement

The unadjusted and adjusted Model 1 analyses did not reveal a significant group difference in the percentage of ocular movement abnormalities (Table 11-10(a,b): $p > 0.42$ for all contrasts). The final adjusted model contained the covariate age.

The unadjusted and adjusted Model 2 results did not detect a significant association between initial dioxin and ocular movement (Table 11-10(c,d), $p > 0.54$ for both analyses). The adjusted analysis contained the covariate insecticide exposure.

For Model 3, the unadjusted analysis of ocular movement did not show any of the Ranch Hand categories to differ significantly from the Comparison group (Table 11-10(e): $p > 0.23$ for all contrasts). The adjusted and unadjusted analyses were identical because no covariates were retained in the final model.

The unadjusted and adjusted analyses for Models 4 through 6 did not reveal a significant association between current dioxin and ocular movement (Table 11-10(g,h): $p > 0.73$ for all analyses). Each of the adjusted models contained the covariate insecticide exposure.

Facial Sensation

The unadjusted and adjusted Model 1 analyses did not show a significant group difference in the percentage of facial sensation abnormalities (Table 11-11(a,b): $p > 0.14$ for all contrasts). No covariates were retained in the adjusted analysis.

For Model 2, the unadjusted analysis did not reveal a significant association between initial dioxin and facial sensation even though the estimated relative risk for a twofold increase in initial dioxin was 1.53 (Table 11-11(c): $p = 0.382$). Only two participants displayed facial sensation abnormalities and both had a high initial dioxin level. The adjusted analysis was not performed due to the sparse number of abnormalities.

The unadjusted Model 3 analysis of facial sensation detected a marginally significant difference between the high Ranch Hands and the Comparisons (Table 11-11(e): $p = 0.076$ from Fisher's exact test). Two of the high Ranch Hands had facial sensation abnormalities whereas none of the Comparisons displayed facial sensation abnormalities. Due to the sparse number of abnormalities, the adjusted Model 3 analysis was not conducted.

For Models 4 through 6, the unadjusted analyses did not find a significant association between current dioxin and facial sensation (Table 11-11(g): $p > 0.24$ for all analyses), although the estimated relative risk for a twofold increase in current dioxin was greater than or equal to 1.47 for each model. Three individuals displayed facial sensation abnormalities in Models 4, 5, and 6. Of the three, two were in the high current dioxin category and the other was in the medium current dioxin category. No covariates were retained in the adjusted analysis.

Table 11-10.
Analysis of Ocular Movement

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***947***	***0.7***	***1.58 (0.53,4.71)***	***0.586***
	Comparison	***1,278***	***0.5***		
Officer	Ranch Hand	367	0.8	1.02 (0.23,4.60)	0.999
	Comparison	501	0.8		
Enlisted Flyer	Ranch Hand	162	0.6	--	0.910
	Comparison	203	0.0		
Enlisted Groundcrew	Ranch Hand	418	0.7	2.07 (0.34,12.43)	0.721
	Comparison	574	0.3		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	***1.56 (0.52,4.67)***	***0.423***	AGE (p=0.094)
Officer	1.01 (0.23,4.55)	0.987	
Enlisted Flyer	--	--	
Enlisted Groundcrew	2.07 (0.35,12.44)	0.425	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

--: Relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

Table 11-10. (Continued)
Analysis of Ocular Movement

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent Abnormal**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	174	1.1	0.80 (0.39,1.67)	0.542
Medium	173	0.6		
High	170	1.2		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
	Analysis Results for Log_2 (Initial Dioxin)[c]		
n	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**	**Covariate Remarks**
517	0.83 (0.40,1.72)	0.609	INS (p=0.121)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 11-10. (Continued)
Analysis of Ocular Movement

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,060	0.5		
Background RH	372	0.5	1.16 (0.22,6.06)	0.863
Low RH	260	1.2	2.41 (0.57,10.21)	0.232
High RH	257	0.8	1.64 (0.31,8.59)	0.556
Low plus High RH	517	1.0	2.03 (0.58,7.11)	0.266

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ab]	p-Value	Covariate Remarks
Comparison	1,060			
Background RH	372	1.16 (0.22,6.06)	0.863	
Low RH	260	2.41 (0.57,10.21)	0.232	
High RH	257	1.64 (0.31,8.59)	0.556	
Low plus High RH	517	2.03 (0.58,7.11)	0.266	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 11-10. (Continued)
Analysis of Ocular Movement

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Abnormal/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	0.7 (293)	1.0 (300)	0.7 (296)	1.07 (0.65,1.76)	0.805
5	0.7 (298)	1.0 (297)	0.7 (294)	1.07 (0.69,1.66)	0.753
6[c]	0.7 (297)	1.0 (297)	0.7 (294)	1.06 (0.66,1.70)	0.810

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	889	1.07 (0.64,1.79)	0.786	INS (p=0.053)
5	889	1.08 (0.69,1.69)	0.735	INS (p=0.052)
6[d]	888	1.07 (0.66,1.72)	0.786	INS (p=0.053)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 11-11.
Analysis of Facial Sensation

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***948***	***0.3***	***4.06 (0.42,39.10)***	***0.419***
	Comparison	***1,280***	***0.1***		
Officer	Ranch Hand	367	0.0	--	--
	Comparison	501	0.0		
Enlisted Flyer	Ranch Hand	162	0.0	--	0.999
	Comparison	203	0.5		
Enlisted Groundcrew	Ranch Hand	419	0.7	--	0.148
	Comparison	576	0.0		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
All	***4.06 (0.42,39.10)***	***0.419***	
Officer	--	--	
Enlisted Flyer	--	0.999	
Enlisted Groundcrew	--	0.148	

--: Relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

Table 11-11. (Continued)
Analysis of Facial Sensation

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent Abnormal**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	174	0.0	1.53 (0.60,3.92)	0.382
Medium	173	0.0		
High	170	1.2		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[a]			
n	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**	**Covariate Remarks**
--	--	--	

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

--: Analysis not performed due to the sparse number of abnormalities.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 11-11. (Continued)
Analysis of Facial Sensation

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value[c]
Comparison	1,062	0.0		
Background RH	373	0.3	--	0.520
Low RH	260	0.0	--	--
High RH	257	0.8	--	0.076
Low plus High RH	517	0.4	--	0.214

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ab]	p-Value	Covariate Remarks
Comparison	--			
Background RH	--	--	--	
Low RH	--	--	--	
High RH	--	--	--	
Low plus High RH	--	--	--	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] P-value equals two times the p-value obtained from Fisher's exact test. This p-value is not adjusted for percent body fat at the time of duty in SEA or change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

--: Analysis not performed due to the sparse number of abnormalities.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 11-11. (Continued)
Analysis of Facial Sensation

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	0.0 (294)	0.3 (300)	0.7 (296)	1.52 (0.76,3.04)	0.251
5	0.0 (299)	0.3 (297)	0.7 (294)	1.47 (0.77,2.78)	0.248
6[c]	0.0 (298)	0.3 (297)	0.7 (294)	1.50 (0.76,2.98)	0.253

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	890	1.52 (0.76,3.04)	0.251	
5	890	1.47 (0.77,2.78)	0.248	
6[c]	889	1.50 (0.76,2.98)	0.253	

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Jaw Clench

Statistical analyses were not performed for jaw clench because there was only one participant with a deviated jaw clench. This individual was an enlisted groundcrew Ranch Hand who was in the high initial dioxin category for Model 2, the high categorized dioxin category for Model 3, and the high current dioxin category for Models 4 through 6. He also was the only participant with an abnormal gag reflex and a deviated palate and uvula movement. Table 11-12(a-d) displays percentages of jaw clench deviations by group and dioxin category.

Smile

The overall prevalence of smile abnormalities did not differ significantly between the Ranch Hand and Comparison groups in the unadjusted Model 1 analyses (Table 11-13(a): $p > 0.10$ for each analysis). Although not significant, the estimated relative risk in the enlisted groundcrew stratum (the occupational cohort with the highest current levels of dioxin) was nearly 7.00 (Table 11-13(a): $p=0.102$, Est. RR=6.94, 95% C.I. = [0.81,59.66]). The nonsignificance of the results must be interpreted with caution due to the sparse number of abnormalities (<1.0% of participants), which leads to decreased statistical power in detecting a significant difference.

To increase statistical power for the enlisted strata, additional unadjusted and adjusted Model 1 analyses were conducted with the enlisted flyers and enlisted groundcrew combined into one stratum. This unadjusted analysis revealed a marginally significant group difference for the enlisted participants (Appendix Table G-5-1(a): $p=0.055$, Est. RR=8.12, 95% C.I.=[0.98, 67.62]). Within the enlisted stratum, the percentages of smile abnormalities for Ranch Hands and Comparisons were 1.0 percent and 0.1 percent respectively. After adjusting for occupation, the adjusted analysis combining enlisted flyers and enlisted groundcrew did not reveal a significant overall group difference (Appendix Table G-5-1(b): $p=0.383$). The relative risk for the enlisted stratum remained marginally significant (Appendix Table G-5-1(b): $p=0.055$, Adj. RR=8.12, 95% C.I.=[0.98, 67.62]).

The unadjusted Model 2 analysis of smile abnormalities did not find a significant association with initial dioxin (Table 11-13(c): $p=0.363$), and the unadjusted Model 3 analysis did not reveal a significant contrast between the Ranch Hand categories and the Comparison group (Table 11-13(e): $p > 0.10$ for all contrasts).

The unadjusted Model 4 analysis found a marginally significant association between lipid-adjusted current dioxin and smile (Table 11-13(g): $p=0.079$, Est. RR=1.49, 95% C.I.=[0.97,2.28]. The association with whole-weight current dioxin was not significant in the unadjusted Model 5 analysis ($p=0.115$) but became marginally significant in the unadjusted Model 6 analysis, which forced total lipids in the model ($p=0.062$, Est. RR=1.51, 95% C.I.=[0.99,2.31]).

All of the adjusted analyses for smile were identical to the unadjusted analyses because no covariates were retained in any of the final adjusted models.

Table 11-12.
Analysis of Jaw Clench

a) MODEL 1: RANCH HANDS VS. COMPARISONS			
Occupational Category	**Group**	**n**	**Percent Deviated**
All	***Ranch Hand***	***948***	***0.1***
	Comparison	***1,280***	***0.0***
Officer	Ranch Hand	367	0.0
	Comparison	501	0.0
Enlisted Flyer	Ranch Hand	162	0.0
	Comparison	203	0.0
Enlisted Groundcrew	Ranch Hand	419	0.2
	Comparison	576	0.0

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN		
Initial Dioxin Category Summary Statistics		
Initial Dioxin	**n**	**Percent Deviated**
Low	174	0.0
Medium	173	0.0
High	170	0.6

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 11-12. (Continued)
Analysis of Jaw Clench

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY		
Dioxin Category	**n**	**Percent Deviated**
Comparison	1,062	0.0
Background RH	373	0.0
Low RH	260	0.0
High RH	257	0.4
Low plus High RH	517	0.2

d) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN			
	Current Dioxin Category Percent Deviated/(n)		
Model[a]	**Low**	**Medium**	**High**
4	0.0 (294)	0.0 (300)	0.3 (296)
5	0.0 (299)	0.0 (297)	0.3 (294)
6	0.0 (298)	0.0 (297)	0.3 (294)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

Note: Model 3: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.
Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 11-13.
Analysis of Smile

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***948***	***0.9***	***1.52 (0.59,3.97)***	***0.533***
	Comparison	***1,280***	***0.6***		
Officer	Ranch Hand	367	0.8	0.58 (0.15,2.26)	0.639
	Comparison	501	1.4		
Enlisted Flyer	Ranch Hand	162	0.6	--	0.910
	Comparison	203	0.0		
Enlisted Groundcrew	Ranch Hand	419	1.2	6.94 (0.81,59.66)	0.102
	Comparison	576	0.2		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.52 (0.59,3.97)***	***0.533***	
Officer	0.58 (0.15,2.26)	0.639	
Enlisted Flyer	--	0.910	
Enlisted Groundcrew	6.94 (0.81,59.66)	0.102	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

--: Relative risk and confidence interval not presented due to the sparse number of abnormalities.

Table 11-13. (Continued)
Analysis of Smile

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent Abnormal**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	174	1.1	1.29 (0.75,2.22)	0.363
Medium	173	0.6		
High	170	1.8		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[a]			
n	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**	**Covariate Remarks**
517	1.29 (0.75,2.22)	0.363	

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 11-13. (Continued)
Analysis of Smile

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,062	0.4		
Background RH	373	0.5	1.58 (0.28,8.75)	0.603
Low RH	260	1.2	2.98 (0.66,13.48)	0.155
High RH	257	1.2	2.84 (0.62,12.94)	0.176
Low plus High RH	517	1.2	2.91 (0.81,10.45)	0.101

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ab]	p-Value	Covariate Remarks
Comparison	1,062			
Background RH	373	1.58 (0.28,8.75)	0.603	
Low RH	260	2.98 (0.66,13.48)	0.155	
High RH	257	2.84 (0.62,12.94)	0.176	
Low plus High RH	517	2.91 (0.81,10.45)	0.101	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 11-13. (Continued)
Analysis of Smile

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Abnormal/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	0.3 (294)	1.3 (300)	1.0 (296)	1.49 (0.97,2.28)	0.079
5	0.3 (299)	1.3 (297)	1.0 (294)	1.38 (0.93,2.05)	0.115
6[c]	0.3 (298)	1.3 (297)	1.0 (294)	1.51 (0.99,2.31)	0.062

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	890	1.49 (0.97,2.28)	0.079	
5	890	1.38 (0.93,2.05)	0.115	
6[c]	889	1.51 (0.99,2.31)	0.062	

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Palpebral Fissure

The unadjusted Model 1 analysis did not find a significant group difference in the percentage of palpebral fissure abnormalities (Table 11-14(a): $p > 0.83$ for all contrasts). The unadjusted and adjusted analyses were identical because no covariates were retained in the final model.

The unadjusted and adjusted Model 2 analyses did not reveal a significant association between initial dioxin and palpebral fissure (Table 11-14(c,d): $p > 0.87$ for both analyses). The adjusted model contained the covariate diabetic class.

The unadjusted Model 3 analysis of palpebral fissure abnormalities did not show any of the Ranch Hand categories to differ significantly from the Comparison group (Table 11-14(e): $p > 0.62$ for all contrasts). The unadjusted analyses for Models 4 through 6 did not reveal any significant associations between current dioxin and palpebral fissure (Table 11-14(g): $p > 0.62$ for all analyses). The adjusted and unadjusted results were identical in Models 3 through 6 because no covariates were retained in the final models.

Balance

The unadjusted and adjusted Model 1 analyses did not reveal a significant group difference in the percentage of balance abnormalities (Table 11-15(a,b): $p > 0.24$ for all contrasts). The nonsignificance of these results must be interpreted with caution due to the sparse number of balance abnormalities (0.5% of participants). Although not significant, the adjusted relative risk for the enlisted groundcrew (the most highly exposed occupational cohort) was nearly 4.00 (Table 11-15(b): $p=0.244$, Adj. RR=3.89, 95% C.I.=[0.40,38.26]). The adjusted analysis contained age and diabetic class.

Initial dioxin was not associated significantly with balance in both the unadjusted and adjusted Model 2 analyses (Table 11-15(c,d): $p > 0.41$ for both analyses). The unadjusted and adjusted Model 3 analyses did not find a significant difference between any of the Ranch Hand categories and the Comparison group (Table 11-15(e,f): $p > 0.53$ for all contrasts). The unadjusted and adjusted analyses for Models 4 through 6 also were not significant (Table 11-15(g,h): $p > 0.45$ for all analyses). Each of the adjusted analyses for Models 2 through 6 contained the covariate age.

Gag Reflex

Statistical analyses for gag reflex were not performed because there was only one participant with an abnormality. This individual also was the only participant with a deviated jaw clench and a deviated palate and uvula movement. Table 11-16(a-d) presents percentages of gag reflex abnormalities by group and dioxin category.

Speech

The unadjusted Model 1 analysis did not reveal a significant group difference in the percentage of speech abnormalities (Table 11-17(a): $p > 0.13$ for all comparisons). Although

Table 11-14.
Analysis of Palpebral Fissure

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***948***	***1.0***	***1.01 (0.43,2.41)***	***0.999***
	Comparison	***1,280***	***0.9***		
Officer	Ranch Hand	367	0.8	0.68 (0.17,2.74)	0.836
	Comparison	501	1.2		
Enlisted Flyer	Ranch Hand	162	1.2	2.53 (0.23,28.10)	0.844
	Comparison	203	0.5		
Enlisted Groundcrew	Ranch Hand	419	1.0	1.01 (0.29,4.12)	0.999
	Comparison	576	0.9		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks**
All	***1.01 (0.43,2.41)***	***0.999***	
Officer	0.68 (0.17,2.74)	0.836	
Enlisted Flyer	2.53 (0.23,28.10)	0.844	
Enlisted Groundcrew	1.01 (0.29,4.12)	0.999	

Table 11-14. (Continued)
Analysis of Palpebral Fissure

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent Abnormal**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	174	0.6	1.05 (0.56,1.98)	0.876
Medium	173	1.2		
High	170	1.2		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**	**Covariate Remarks**
517	1.04 (0.55,1.94)	0.909	DIAB (p=0.080)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 11-14. (Continued)
Analysis of Palpebral Fissure

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,062	0.8		
Background RH	373	1.1	1.35 (0.41,4.46)	0.624
Low RH	260	1.2	1.35 (0.36,5.04)	0.657
High RH	257	0.8	0.86 (0.18,4.04)	0.848
Low plus High RH	517	1.0	1.10 (0.36,3.32)	0.866

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ab]	p-Value	Covariate Remarks
Comparison	1,062			
Background RH	373	1.35 (0.41,4.46)	0.624	
Low RH	260	1.35 (0.36,5.04)	0.657	
High RH	257	0.86 (0.18,4.04)	0.848	
Low plus High RH	517	1.10 (0.36,3.32)	0.866	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤10 ppt.
Background (Ranch Hand): Current Dioxin ≤10 ppt.
Low (Ranch Hand): Current Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤143 ppt.
High (Ranch Hand): Current Dioxin >10 ppt, Initial Dioxin >143 ppt.

Table 11-14. (Continued)
Analysis of Palpebral Fissure

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	0.7 (294)	1.7 (300)	0.7 (296)	1.09 (0.70,1.68)	0.717
5	1.0 (299)	1.3 (297)	0.7 (294)	1.06 (0.72,1.56)	0.761
6[c]	1.0 (298)	1.3 (297)	0.7 (294)	1.11 (0.73,1.68)	0.629

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	890	1.09 (0.70,1.68)	0.717	
5	890	1.06 (0.72,1.56)	0.761	
6[c]	889	1.11 (0.73,1.68)	0.629	

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 11-15.
Analysis of Balance

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***947***	***0.5***	***1.13 (0.34,3.70)***	***0.999***
	Comparison	***1,279***	***0.5***		
Officer	Ranch Hand	366	0.5	1.37 (0.19,9.76)	0.999
	Comparison	500	0.4		
Enlisted Flyer	Ranch Hand	162	0.0	--	0.332
	Comparison	203	1.5		
Enlisted Groundcrew	Ranch Hand	419	0.7	4.15 (0.43,40.01)	0.408
	Comparison	576	0.2		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.03 (0.31,3.43)***	***0.960***	AGE (p=0.022) DIAB (p=0.006)
Officer	1.18 (0.16,8.55)	0.872	
Enlisted Flyer	--	--	
Enlisted Groundcrew	3.89 (0.40,38.26)	0.244	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

--: Relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

Table 11-15. (Continued)
Analysis of Balance

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent Abnormal**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	174	0.6	1.14 (0.51,2.51)	0.757
Medium	172	0.0		
High	170	1.2		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**	**Covariate Remarks**
516	1.42 (0.63,3.19)	0.414	AGE (p=0.059)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 11-15. (Continued)
Analysis of Balance

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,061	0.5		
Background RH	373	0.5	1.19 (0.23,6.29)	0.836
Low RH	259	0.4	0.71 (0.08,6.15)	0.755
High RH	257	0.8	1.31 (0.23,7.41)	0.760
Low plus High RH	516	0.6	1.01 (0.23,4.43)	0.994

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,061			AGE (p=0.023)
Background RH	373	1.10 (0.21,5.83)	0.912	
Low RH	259	0.61 (0.07,5.45)	0.662	
High RH	257	1.72 (0.31,9.61)	0.539	
Low plus High RH	516	1.06 (0.24,4.70)	0.935	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 11-15. (Continued)
Analysis of Balance

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	0.3 (294)	0.7 (300)	0.7 (295)	1.08 (0.60,1.95)	0.788
5	0.3 (299)	0.3 (296)	1.0 (294)	1.10 (0.66,1.84)	0.717
6[c]	0.3 (298)	0.3 (296)	1.0 (294)	1.05 (0.60,1.83)	0.877

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	889	1.26 (0.66,2.42)	0.490	AGE (p=0.014)
5	889	1.25 (0.70,2.22)	0.455	AGE (p=0.013)
6[d]	888	1.20 (0.65,2.24)	0.565	AGE (p=0.014)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 11-16.
Analysis of Gag Reflex

a) MODEL 1: RANCH HANDS VS. COMPARISONS			
Occupational Category	**Group**	**n**	**Percent Abnormal**
All	***Ranch Hand***	***948***	***0.1***
	Comparison	***1,280***	***0.0***
Officer	Ranch Hand	367	0.0
	Comparison	501	0.0
Enlisted Flyer	Ranch Hand	162	0.0
	Comparison	203	0.0
Enlisted Groundcrew	Ranch Hand	419	0.2
	Comparison	576	0.0

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN		
Initial Dioxin Category Summary Statistics		
Initial Dioxin	**n**	**Percent Abnormal**
Low	174	0.0
Medium	173	0.0
High	170	0.6

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 11-16. (Continued)
Analysis of Gag Reflex

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY		
Dioxin Category	**n**	**Percent Abnormal**
Comparison	1,062	0.0
Background RH	373	0.0
Low RH	260	0.0
High RH	257	0.4
Low plus High RH	517	0.2

d) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN			
	Current Dioxin Category Percent Abnormal/(n)		
Model[a]	**Low**	**Medium**	**High**
4	0.0 (294)	0.0 (300)	0.3 (296)
5	0.0 (299)	0.0 (297)	0.3 (294)
6	0.0 (298)	0.0 (297)	0.3 (294)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

Note: Model 3: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.
Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

none of the contrasts were significant, the estimated relative risk for the overall group contrast exceeded 4.00, and the estimated relative risk within the enlisted groundcrew stratum was greater than 5.00 (Table 11-17(a): p=0.133, Est. RR=4.07, 95% C.I.=[0.82,20.21]; p=0.205, Est. RR=5.54, 95% C.I.=[0.62,49.77] respectively). These results should be interpreted with caution due to the sparse number of abnormalities.

To increase statistical power for the enlisted strata, additional unadjusted and adjusted Model 1 analyses were conducted with the enlisted flyers and enlisted groundcrew combined into one stratum. This unadjusted analysis did not reveal a significant difference between the Ranch Hands and Comparisons (Appendix Table G-5-2(a): $p > 0.10$ for all contrasts) even though the estimated relative risk for the enlisted stratum was greater than 6 (Appendix Table G-5-2(a): p=0.109, Est. RR=6.75, 95% C.I.=[0.79, 57.96]). The adjusted analysis combining enlisted flyers and enlisted groundcrew revealed a marginally significant overall group difference in the percentage of speech abnormalities (Table G-5-2(b): p=0.068, Adj. RR=3.98, 95% C.I.=[0.80, 19.91]). Stratifying by occupation also revealed a marginally significant group difference for the enlisted participants (Table G-5-2(b): p=0.090, Adj. RR=6.55, 95% C.I.=[0.74, 57.62]). The final model for this adjusted analysis contained the covariates age and occupation.

After adjusting for age, the overall group contrast in the Model 1 analysis of speech abnormalities became marginally significant (Table 11-17(b): p=0.063, Adj. RR=4.06, 95% C.I.=[0.81,20.20]). The relative risk for the enlisted groundcrew remained greater than 5.00 and nonsignificant in the adjusted analysis (Table 11-17(b): p=0.132, Adj. RR=5.45, 95% C.I.=[0.60,49.56]).

The unadjusted and adjusted Model 2 analyses did not reveal a significant association between initial dioxin and speech (Table 11-17(c,d): $p \geq 0.47$ for both analyses). Age was the only covariate retained in the adjusted analysis.

The unadjusted Model 3 analysis revealed significantly or marginally significantly more speech abnormalities in the low, high, and low plus high Ranch Hand categories than in the Comparison group (Table 11-17(e): p=0.077, p=0.076, and p=0.023 respectively). There were no speech abnormalities in the Comparison group and two speech abnormalities (0.8%) in each of the low and high categories. Relative risk estimates were not calculated because there were no abnormalities in the Comparison group. The statistical significance of these results should be interpreted with caution because the analysis was not adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin. An adjusted analysis was not conducted because the Comparison group had no abnormalities.

The unadjusted and adjusted analyses for Models 4 through 6 did not show a significant association between current dioxin and speech (Table 11-17(g,h): $p > 0.44$ for all analyses). Each of the adjusted analyses contained age and occupation.

Table 11-17.
Analysis of Speech

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***948***	***0.6***	***4.07 (0.82,20.21)***	***0.133***
	Comparison	***1,280***	***0.2***		
Officer	Ranch Hand	367	0.3	1.37 (0.09,21.91)	0.999
	Comparison	501	0.2		
Enlisted Flyer	Ranch Hand	162	0.6	--	0.910
	Comparison	203	0.0		
Enlisted Groundcrew	Ranch Hand	419	1.0	5.54 (0.62,49.77)	0.205
	Comparison	576	0.2		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***4.06 (0.81,20.20)***	***0.063***	AGE (p=0.004)
Officer	1.40 (0.09,22.59)	0.814	
Enlisted Flyer	--	--	
Enlisted Groundcrew	5.45 (0.60,49.56)	0.132	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

--: Relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

Table 11-17. (Continued)
Analysis of Speech

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent Abnormal**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	174	0.6	1.11 (0.54,2.26)	0.777
Medium	173	0.6		
High	170	1.2		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
	Analysis Results for Log_2 (Initial Dioxin)[c]		
n	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**	**Covariate Remarks**
517	1.33 (0.63,2.79)	0.470	AGE (p=0.089)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 11-17. (Continued)
Analysis of Speech

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value[b]
Comparison	1,062	0.0		
Background RH	373	0.3	--	0.520
Low RH	260	0.8	--	0.077
High RH	257	0.8	--	0.076
Low plus High RH	517	0.8	--	0.023

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
Comparison	--			
Background RH	--	--	--	
Low RH	--	--	--	
High RH	--	--	--	
Low plus High RH	--	--	--	

[a] Relative risk and confidence interval relative to Comparisons.

[b] P-value equals two times the p-value obtained from a one-sided Fisher's exact test. This p-value is not adjusted for percent body fat at the time of duty in SEA or change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

--: Adjusted relative risk and confidence interval not presented due to the sparse number of abnormalities; adjusted analyses not performed due to the sparse number of abnormalities.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$ 10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin $\leq$ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 11-17. (Continued)
Analysis of Speech

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Abnormal/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	0.3 (294)	0.7 (300)	0.7 (296)	1.24 (0.71,2.18)	0.461
5	0.3 (299)	0.7 (297)	0.7 (294)	1.22 (0.73,2.03)	0.446
6[c]	0.3 (298)	0.7 (297)	0.7 (294)	1.21 (0.70,2.10)	0.490

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	890	1.05 (0.57,1.92)	0.882	AGE (p=0.014) OCC (p=0.034)
5	890	1.05 (0.62,1.78)	0.858	AGE (p=0.014) OCC (p=0.034)
6[d]	889	1.04 (0.58,1.85)	0.903	AGE (p=0.014) OCC (p=0.034)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids .

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Palate and Uvula Movement

Statistical analyses were not conducted because there was only one participant with a deviated palate and uvula movement. This individual also was the only participant with a deviated jaw clench and an abnormal gag reflex. Table 11-18(a-d) displays percentages of deviated palate and uvula movement by group and dioxin category.

Neck Range of Motion

The unadjusted Model 1 analysis of neck range of motion did not show the Ranch Hands and Comparisons to differ significantly (Table 11-19(a): $p>0.14$ for all contrasts). The relative risk for the overall group contrast remained nonsignificant after adjusting for age, race, and occupation (Table 11-19(b): $p=0.919$). However, stratifying the adjusted analysis by occupation revealed a marginally significant group difference within the enlisted flyer stratum (Table 11-19(b): $p=0.067$, Adj. RR=0.58, 95% C.I.=[0.33,1.04]). For the enlisted flyers, Ranch Hands had fewer abnormalities than Comparisons (Table 11-19(a): 14.2% versus 20.7%).

The unadjusted and adjusted Model 2 analyses did not reveal a significant association between initial dioxin and neck range of motion (Table 11-19(c,d): $p\geq0.34$ for both analyses). The adjusted final model contained diabetic class and an age-by-occupation interaction.

The unadjusted Model 3 analysis of neck range of motion did not show a significant contrast between any of the Ranch Hand categories and the Comparison group (Table 11-19(e): $p>0.44$ for all contrasts). The categorized dioxin-by-occupation interaction was retained in the adjusted Model 3 analysis (Table 11-19(f): $p=0.021$). Appendix Table G-2-4 presents adjusted results stratified by occupation. In addition to this interaction, the final adjusted model included age. When the categorized dioxin-by-occupation interaction was removed from the final model, the adjusted analysis did not reveal any significant contrasts (Table 11-19(f): $p>0.22$ for all contrasts).

For Models 4 through 6, the unadjusted and adjusted analyses did not detect a significant association between current dioxin and neck range of motion (Table 11-19(g,h): $p>0.11$ for all analyses). Each of the adjusted analyses contained insecticide exposure and two covariate-by-covariate interactions: age-by-occupation and occupation-by-lifetime alcohol history. The adjusted relative risk for lipid-adjusted current dioxin and for whole-weight current dioxin became significantly greater than 1.00 in Models 4 and 5 when occupation was removed from both of the final models (Appendix Table G-3-5(c): $p=0.049$, Adj. RR=1.16, 95% C.I.=[1.00,1.35] for Model 4; $p=0.045$, Adj. RR=1.14, 95% C.I.=[1.00,1.29] for Model 5). The adjusted relative risk for whole-weight dioxin became marginally greater than 1.00 when total lipids was forced into the adjusted Model 6 analysis excluding occupation ($p=0.075$, Adj. RR=1.13, 95% C.I.=[0.99,1.30]).

Table 11-18.
Analysis of Palate and Uvula Movement

a) MODEL 1: RANCH HANDS VS. COMPARISONS			
Occupational Category	**Group**	**n**	**Percent Deviated**
All	***Ranch Hand***	***948***	***0.1***
	Comparison	***1,280***	***0.0***
Officer	Ranch Hand	367	0.0
	Comparison	501	0.0
Enlisted Flyer	Ranch Hand	162	0.0
	Comparison	203	0.0
Enlisted Groundcrew	Ranch Hand	419	0.2
	Comparison	576	0.0

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN		
Initial Dioxin Category Summary Statistics		
Initial Dioxin	**n**	**Percent Deviated**
Low	174	0.0
Medium	173	0.0
High	170	0.6

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 11-18. (Continued)
Analysis of Palate and Uvula Movement

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY		
Dioxin Category	**n**	**Percent Deviated**
Comparison	1,062	0.0
Background RH	373	0.0
Low RH	260	0.0
High RH	257	0.4
Low plus High RH	517	0.2

d) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN			
	Current Dioxin Category Percent Deviated/(n)		
Model[a]	**Low**	**Medium**	**High**
4	0.0 (294)	0.0 (300)	0.3 (296)
5	0.0 (299)	0.0 (297)	0.3 (294)
6	0.0 (298)	0.0 (297)	0.3 (294)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

Note: Model 3: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.
Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 11-19.
Analysis of Neck Range of Motion

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***947***	***14.4***	***1.04 (0.82,1.32)***	***0.808***
	Comparison	***1,280***	***13.9***		
Officer	Ranch Hand	367	18.3	1.19 (0.83,1.71)	0.381
	Comparison	501	15.8		
Enlisted Flyer	Ranch Hand	162	14.2	0.63 (0.36,1.11)	0.141
	Comparison	203	20.7		
Enlisted Groundcrew	Ranch Hand	418	11.0	1.13 (0.75,1.70)	0.645
	Comparison	576	9.9		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.01 (0.79,1.31)***	***0.919***	AGE ($p<0.001$) RACE ($p=0.039$) OCC ($p=0.144$)
Officer	1.19 (0.82,1.74)	0.362	
Enlisted Flyer	0.58 (0.33,1.04)	0.067	
Enlisted Groundcrew	1.14 (0.73,1.76)	0.571	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 11-19. (Continued)
Analysis of Neck Range of Motion

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent Abnormal**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	174	17.2	0.91 (0.76,1.10)	0.340
Medium	173	12.7		
High	169	14.2		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
	Analysis Results for Log_2 (Initial Dioxin)[c]		
n	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**	**Covariate Remarks**
516	1.02 (0.81,1.29)	0.867	DIAB (p=0.117) AGE*OCC (p=0.022)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 11-19. (Continued)
Analysis of Neck Range of Motion

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,062	13.2		
Background RH	373	13.4	1.07 (0.75,1.52)	0.702
Low RH	260	15.8	1.16 (0.79,1.70)	0.446
High RH	256	13.7	1.01 (0.67,1.51)	0.976
Low plus High RH	516	14.7	1.08 (0.80,1.47)	0.605

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	1,062			DXCAT*OCC (p=0.021) AGE (p=0.023)
Background RH	373	0.98 (0.68,1.42)**	0.919**	
Low RH	260	1.04 (0.70,1.56)**	0.836**	
High RH	256	1.32 (0.84,2.05)**	0.225**	
Low plus High RH	516	1.15 (0.83,1.59)**	0.399**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table G-2-4 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 11-19. (Continued)
Analysis of Neck Range of Motion

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Abnormal/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	12.6 (294)	17.0 (300)	12.9 (295)	1.01 (0.89,1.15)	0.832
5	12.7 (299)	15.8 (297)	14.0 (293)	1.03 (0.92,1.15)	0.650
6[c]	12.8 (298)	15.8 (297)	14.0 (293)	1.00 (0.89,1.13)	0.968

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	869	1.14 (0.96,1.35)	0.127	INS (p=0.124) AGE*OCC (p<0.001) OCC*DRKYR (p=0.008)
5	869	1.12 (0.97,1.30)	0.112	INS (p=0.123) AGE*OCC (p<0.001) OCC*DRKYR (p=0.008)
6[d]	868	1.12 (0.95,1.31)	0.166	INS (p=0.123) AGE*OCC (p<0.001) OCC*DRKYR (p=0.008)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Cranial Nerve Index without Range of Motion

The unadjusted Model 1 analysis of the cranial nerve index without range of motion did not show a significant overall group difference (Table 11-20(a): $p=0.266$). However, stratifying the unadjusted analysis by occupation revealed a significant group difference within the enlisted groundcrew stratum (Table 11-20(a): $p=0.012$, Est. RR=2.44, 95% C.I.=[1.25,4.78]). Ranch Hand enlisted groundcrew were more than twice as likely as Comparison enlisted groundcrew to have abnormalities (5.8% versus 2.4%).

The adjusted Model 1 analysis contained a significant interaction between group and occupation (Table 11-20(b): $p=0.034$). In addition to this interaction, the final model included four covariates: age, lifetime alcohol history, insecticide exposure, and diabetic class. The adjusted relative risk for the overall group contrast was not significant when the group-by-occupation interaction was removed from the final model (Table 11-20(b): $p=0.395$). The relative risk for the enlisted groundcrew remained significant when the adjusted analysis was stratified by occupation (Table 11-20(b): $p=0.014$, Adj. RR=2.36, 95% C.I.=[1.19,4.71].

For Model 2, the unadjusted analysis did not reveal a significant association between initial dioxin and the cranial nerve index without range of motion (Table 11-20(c): $p=0.619$). The adjusted Model 2 analysis retained initial dioxin-by-age and initial dioxin-by-diabetic class interactions (Table 11-20(d): $p=0.033$ and $p=0.003$ respectively). Appendix Table G-2-5 presents adjusted results stratified separately by age and diabetic class. After removing the initial dioxin-by-age and initial dioxin-by-diabetic class interactions from the final model, the adjusted Model 2 analysis did not reveal a significant association between initial dioxin and cranial nerve index without range of motion (Table 11-20(d): $p=0.335$).

The unadjusted Model 3 analysis of the cranial nerve index without range of motion did not find a significant difference between any of the Ranch Hand categories and the Comparison group (Table 11-20(e): $p>0.11$ for all contrasts). The interaction between categorized dioxin and occupation was included in the adjusted Model 3 analysis (Table 11-20(d): $p=0.017$). Appendix Table G-2-5 presents adjusted results stratified by occupation. In addition to the categorized dioxin-by-occupation interaction, the adjusted analysis contained age, diabetic class, and insecticide exposure. Without the categorized dioxin-by-occupation interaction in the final model, the adjusted Model 3 analysis did not show any of the Ranch Hand categories to be significantly different from the Comparison group (Table 11-20(f): $p>0.25$ for all contrasts).

The unadjusted and adjusted analyses for Models 4 through 6 did not reveal a significant association between current dioxin and the cranial nerve index without range of motion (Table 11-20(g,h): $p>0.68$ for all analyses). Each of the adjusted analyses contained age, occupation, and a diabetic class-by-insecticide exposure interaction.

Table 11-20.
Analysis of Cranial Nerve Index without Range of Motion

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***945***	***4.6***	***1.30 (0.85,2.00)***	***0.266***
	Comparison	***1,276***	***3.5***		
Officer	Ranch Hand	366	3.8	0.86 (0.44,1.71)	0.801
	Comparison	499	4.4		
Enlisted Flyer	Ranch Hand	162	3.1	0.69 (0.23,2.09)	0.695
	Comparison	203	4.4		
Enlisted Groundcrew	Ranch Hand	417	5.8	2.44 (1.25,4.78)	0.012
	Comparison	574	2.4		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.21 (0.78,1.87)*****	***0.395*****	GROUP*OCC (p=0.034)
Officer	0.79 (0.39,1.57)	0.495	AGE (p<0.001)
Enlisted Flyer	0.62 (0.20,1.91)	0.404	DRKYR (p=0.138)
Enlisted Groundcrew	2.36 (1.19,4.71)	0.014	INS (p=0.019) DIAB (p=0.014)

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

Table 11-20. (Continued)
Analysis of Cranial Nerve Index without Range of Motion

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	174	5.7	1.08 (0.80,1.46)	0.619
Medium	172	2.3		
High	169	6.5		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
515	1.19 (0.84,1.70)**	0.335**	INIT*AGE (p=0.033) INIT*DIAB (p=0.003)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interactions ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table G-2-5 for further analysis of these interactions.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 11-20. (Continued)
Analysis of Cranial Nerve Index without Range of Motion

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,058	3.3		
Background RH	372	4.3	1.32 (0.72,2.43)	0.368
Low RH	259	5.4	1.66 (0.88,3.14)	0.119
High RH	256	4.3	1.31 (0.65,2.62)	0.450
Low plus High RH	515	4.9	1.48 (0.88,2.51)	0.142

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,057			DXCAT*OCC (p=0.017) AGE (p=0.002) DIAB (p=0.131) INS (p=0.037)
Background RH	371	1.26 (0.67,2.36)**	0.476**	
Low RH	259	1.46 (0.76,2.79)**	0.255**	
High RH	256	1.27 (0.61,2.62)**	0.520**	
Low plus High RH	515	1.37 (0.80,2.35)**	0.253**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table G-2-5 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 11-20. (Continued)
Analysis of Cranial Nerve Index without Range of Motion

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Abnormal/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	4.1 (293)	5.7 (300)	4.1 (294)	1.05 (0.84,1.29)	0.683
5	4.4 (298)	5.1 (296)	4.4 (293)	1.03 (0.85,1.24)	0.782
6[c]	4.4 (297)	5.1 (296)	4.4 (293)	1.02 (0.83,1.24)	0.884

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	886	0.97 (0.77,1.24)	0.815	AGE (p=0.049) OCC (p=0.020) DIAB*INS (p=0.013)
5	886	0.96 (0.79,1.18)	0.713	AGE (p=0.050) OCC (p=0.017) DIAB*INS (p=0.013)
6[d]	885	0.96 (0.77,1.19)	0.693	AGE (p=0.050) OCC (p=0.018) DIAB*INS (p=0.013)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Physical Examination Variables: Peripheral Nerve Status

Pin Prick

The unadjusted and adjusted Model 1 analyses of pin prick did not reveal a significant difference between the Ranch Hands and Comparisons (Table 11-21(a,b): $p>0.19$ for all contrasts). The adjusted model retained age and diabetic class.

The unadjusted and adjusted analyses for Model 2 did not reveal a significant association between initial dioxin and pin prick (Table 11-21(c,d): $p>0.60$ for both analyses). The adjusted analysis included diabetic class and an age-by-occupation interaction.

The unadjusted and adjusted Model 3 results of pin prick analyses did not show any of the Ranch Hand categories to be significantly different from the Comparison group (Table 11-21(e,f): $p>0.36$ for all contrasts). Age and diabetic class were significant covariates in the adjusted analysis.

The unadjusted analyses for Models 4 through 6 revealed a marginally significant positive association between current dioxin and pin prick (Table 11-21(g): $p=0.079$, Est. RR=1.19, 95% C.I.=[0.98,1.44]; $p=0.064$, Est. RR=1.18, 95% C.I.=[0.99,1.40]; and $p=0.079$, Est. RR=1.18, 95% C.I.=[0.98,1.42] for Models 4, 5, and 6 respectively).

Each of the adjusted analyses for Models 4 through 6 contained a significant current dioxin-by-diabetic class interaction (Table 11-21(h): $p=0.006$, $p=0.014$, and $p=0.011$ for Models 4, 5, and 6 respectively). Appendix Table G-2-6 presents adjusted results stratified by diabetic class for each of the three models. In addition to the current dioxin-by-diabetic class interaction, each of the adjusted analyses for Models 4 through 6 included two covariate-by-covariate interactions: age-by-occupation and occupation-by-diabetic class. In contrast to the unadjusted results, the adjusted analyses of Models 4 through 6 did not reveal a significant association between current dioxin and pin prick when the current dioxin-by-diabetic class interaction was removed from each of the adjusted models ($p>0.18$).

The adjusted results for Models 4 through 6 changed when occupation and diabetic class were removed from the final models. Without occupation and diabetic class, each of the adjusted analyses revealed a significant positive association between current dioxin and pin prick (Appendix Table G-3-7(c): $p=0.014$, Adj. RR=1.30, 95% C.I.=[1.06,1.59]; $p=0.013$, Adj. RR=1.26, 95% C.I.=[1.05,1.52]; and $p=0.014$, Adj. RR=1.28, 95% C.I.=[1.05, 1.57] for Models 4, 5, and 6 respectively).

Light Touch

For Model 1, the unadjusted and adjusted analyses of light touch did not show a significant difference between Ranch Hands and Comparisons (Table 11-22(a,b): $p>0.13$ for all contrasts). The adjusted model included age, diabetic class, and lifetime alcohol history.

Table 11-21.
Analysis of Pin Prick

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***908***	***5.5***	***1.02 (0.70,1.48)***	***0.999***
	Comparison	***1,217***	***5.4***		
Officer	Ranch Hand	348	5.5	0.99 (0.54,1.82)	0.999
	Comparison	473	5.5		
Enlisted Flyer	Ranch Hand	156	5.1	0.57 (0.24,1.35)	0.275
	Comparison	195	8.7		
Enlisted Groundcrew	Ranch Hand	404	5.7	1.38 (0.76,2.50)	0.359
	Comparison	549	4.2		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***0.98 (0.67,1.43)***	***0.911***	AGE ($p<0.001$) DIAB ($p=0.003$)
Officer	0.93 (0.50,1.72)	0.819	
Enlisted Flyer	0.56 (0.23,1.34)	0.194	
Enlisted Groundcrew	1.36 (0.74,2.48)	0.317	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 11-21. (Continued)
Analysis of Pin Prick

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	163	6.7	0.97 (0.74,1.27)	0.832
Medium	165	6.1		
High	163	6.1		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
491	0.92 (0.66,1.28)	0.604	DIAB (p=0.034) AGE*OCC (p=0.022)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 11-21. (Continued)
Analysis of Pin Prick

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,013	5.4		
Background RH	361	4.4	0.93 (0.52,1.65)	0.795
Low RH	245	7.3	1.29 (0.74,2.26)	0.363
High RH	246	5.3	0.86 (0.46,1.62)	0.642
Low plus High RH	491	6.3	1.07 (0.68,1.70)	0.768

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,013			AGE (p=0.003) DIAB (p=0.039)
Background RH	360	0.88 (0.49,1.58)	0.672	
Low RH	245	1.19 (0.68,2.08)	0.552	
High RH	246	0.92 (0.49,1.75)	0.803	
Low plus High RH	491	1.06 (0.67,1.69)	0.804	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 11-21. (Continued)
Analysis of Pin Prick

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	2.8 (285)	8.5 (284)	5.3 (283)	1.19 (0.98,1.44)	0.079
5	3.8 (292)	6.8 (279)	6.0 (281)	1.18 (0.99,1.40)	0.064
6[c]	3.8 (291)	6.8 (279)	6.0 (281)	1.18 (0.98,1.42)	0.079

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	851	1.17 (0.91,1.50)**	0.220**	CURR*DIAB (p=0.006) AGE*OCC (p=0.025) OCC*DIAB (p=0.002)
5	851	1.15 (0.93,1.43)**	0.195**	CURR*DIAB (p=0.014) AGE*OCC (p=0.021) OCC*DIAB (p=0.003)
6[d]	850	1.17 (0.92,1.48)**	0.186**	CURR*DIAB (p=0.011) AGE*OCC (p=0.032) OCC*DIAB (p=0.003)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table G-2-6 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 11-22.
Analysis of Light Touch

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***908***	***5.1***	***1.33 (0.88,2.01)***	***0.217***
	Comparison	***1,217***	***3.9***		
Officer	Ranch Hand	348	4.6	1.09 (0.56,2.14)	0.934
	Comparison	473	4.2		
Enlisted Flyer	Ranch Hand	156	4.5	1.10 (0.39,3.10)	0.999
	Comparison	195	4.1		
Enlisted Groundcrew	Ranch Hand	404	5.7	1.68 (0.90,3.14)	0.134
	Comparison	549	3.5		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.23 (0.80,1.88)***	***0.347***	AGE ($p<0.001$) DIAB ($p=0.060$) DRKYR ($p=0.149$)
Officer	0.80 (0.44,1.46)	0.465	
Enlisted Flyer	1.07 (0.46,2.47)	0.874	
Enlisted Groundcrew	1.26 (0.73,2.16)	0.413	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 11-22. (Continued)
Analysis of Light Touch

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	163	4.9	0.97 (0.72,1.29)	0.821
Medium	165	6.7		
High	163	4.9		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[a]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
491	0.97 (0.72,1.29)	0.821	

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 11-22. (Continued)
Analysis of Light Touch

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,013	4.1		
Background RH	361	4.4	1.23 (0.68,2.23)	0.500
Low RH	245	5.7	1.30 (0.69,2.43)	0.412
High RH	246	5.3	1.15 (0.60,2.19)	0.678
Low plus High RH	491	5.5	1.22 (0.74,2.02)	0.433

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,013			AGE ($p<0.001$)
Background RH	361	1.15 (0.63,2.09)	0.646	
Low RH	245	1.22 (0.65,2.28)	0.544	
High RH	246	1.33 (0.69,2.56)	0.394	
Low plus High RH	491	1.27 (0.76,2.10)	0.358	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$ 10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$ 10 ppt.
Low (Ranch Hand): Current Dioxin $>$ 10 ppt, 10 ppt $<$ Initial Dioxin $\leq$ 143 ppt.
High (Ranch Hand): Current Dioxin $>$ 10 ppt, Initial Dioxin $>$ 143 ppt.

Table 11-22. (Continued)
Analysis of Light Touch

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	3.5 (285)	6.3 (284)	5.3 (283)	1.12 (0.92,1.38)	0.264
5	4.1 (292)	4.7 (279)	6.4 (281)	1.14 (0.95,1.36)	0.165
6[c]	4.1 (291)	4.7 (279)	6.4 (281)	1.10 (0.91,1.34)	0.335

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	851	1.15 (0.89,1.48)	0.272	AGE (p=0.013) OCC*DIAB (p=0.016)
5	851	1.15 (0.93,1.44)	0.192	AGE (p=0.013) OCC*DIAB (p=0.016)
6[d]	850	1.14 (0.90,1.44)	0.284	AGE (p=0.013) OCC*DIAB (p=0.016)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

The unadjusted Model 2 analysis did not show a significant association between light touch and initial dioxin (Table 11-22(c): $p=0.821$). The adjusted results were identical to the unadjusted results because no covariates were retained in the final model.

Both the unadjusted and adjusted analyses of light touch for Model 3 detected no significant contrasts involving the Comparisons (Table 11-22(e,f): $p>0.35$ for all contrasts). Age was significant in the adjusted analysis.

The unadjusted and adjusted results for Models 4 through 6 revealed no significant association between current dioxin and light touch (Table 11-22(g,h): $p>0.16$ for all analyses). Each of the adjusted models contained age and an occupation-by-diabetic class interaction.

The adjusted results for Models 4 and 5 changed when occupation and diabetic class were removed from the final models. Without these two covariates, the adjusted analyses revealed a marginally significant and a significant positive association between current dioxin and light touch for Models 4 and 5 respectively (Appendix Table G-3-8(a): $p=0.079$, Adj. RR=1.22, 95% C.I.=[0.98,1.51] and $p=0.049$, Adj. RR=1.21, 95% C.I.=[1.00,1.47] for Models 4 and 5).

Muscle Status

For Model 1, the unadjusted and adjusted analyses did not reveal a significant group difference in the percentage of abnormalities for muscle status (Table 11-23(a,b): $p>0.15$ for all contrasts). Age and race were significant covariates in the final adjusted model.

The unadjusted and adjusted Model 2 analyses did not detect a significant association between initial dioxin and muscle status (Table 11-23(c,d): $p>0.63$ for both analyses). The final model contained the covariate age.

The unadjusted Model 3 analysis of muscle status did not show any of the Ranch Hand categories to be significantly different from the Comparison group (Table 11-23(e): $p>0.42$ for all contrasts). The adjusted analysis for Model 3 included a significant interaction between categorized dioxin and insecticide exposure (Table 11-23(f): $p=0.024$). Appendix Table G-2-7 displays adjusted results stratified by insecticide exposure. When the categorized dioxin-by-insecticide exposure interaction was removed from the final model, which retained age and race, the adjusted analysis did not show a significant difference between Ranch Hands and Comparisons (Table 11-23(f): $p>0.31$ for all contrasts).

The unadjusted and adjusted results for Models 4 through 6 did not reveal a significant association between current dioxin and muscle status (Table 11-23(g,h): $p>0.60$ for all analyses). Each of the adjusted analyses contained age and race.

Patellar Reflex

The unadjusted Model 1 analysis revealed a significant overall group difference in the percentage of patellar reflex abnormalities (Table 11-24(a): $p=0.043$, Est. RR=0.48, 95%

Table 11-23.
Analysis of Muscle Status

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***948***	***3.4***	***1.32 (0.80,2.16)***	***0.331***
	Comparison	***1,278***	***2.6***		
Officer	Ranch Hand	367	3.3	1.51 (0.66,3.45)	0.448
	Comparison	501	2.2		
Enlisted Flyer	Ranch Hand	162	3.1	0.61 (0.20,1.82)	0.526
	Comparison	201	5.0		
Enlisted Groundcrew	Ranch Hand	419	3.6	1.75 (0.81,3.77)	0.216
	Comparison	576	2.1		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.31 (0.80,2.14)***	***0.291***	AGE (p=0.010) RACE (p=0.008)
Officer	1.50 (0.65,3.44)	0.340	
Enlisted Flyer	0.59 (0.20,1.76)	0.340	
Enlisted Groundcrew	1.75 (0.81,3.78)	0.158	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 11-23. (Continued)
Analysis of Muscle Status

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	174	2.9	0.98 (0.67,1.42)	0.905
Medium	173	3.5		
High	170	2.9		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
517	1.10 (0.74,1.62)	0.637	AGE (p=0.035)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 11-23. (Continued)
Analysis of Muscle Status

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,062	2.5		
Background RH	373	3.2	1.16 (0.58,2.33)	0.674
Low RH	260	3.1	1.25 (0.56,2.79)	0.590
High RH	257	3.1	1.34 (0.60,3.00)	0.477
Low plus High RH	517	3.1	1.29 (0.69,2.43)	0.427

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,062			DXCAT*INS (p=0.024) AGE (p=0.013) RACE (p=0.015)
Background RH	373	1.08 (0.54,2.19)**	0.821**	
Low RH	260	1.26 (0.56,2.85)**	0.578**	
High RH	257	1.52 (0.67,3.44)**	0.317**	
Low plus High RH	517	1.38 (0.73,2.61)**	0.327**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table G-2-7 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 11-23. (Continued)
Analysis of Muscle Status

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Abnormal/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	3.4 (294)	2.7 (300)	3.4 (296)	0.99 (0.76,1.28)	0.923
5	3.3 (299)	2.7 (297)	3.4 (294)	0.99 (0.80,1.24)	0.954
6[c]	3.4 (298)	2.7 (297)	3.4 (294)	1.00 (0.78,1.27)	0.971

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	890	1.06 (0.81,1.40)	0.661	AGE (p=0.006) RACE (p=0.100)
5	890	1.05 (0.83,1.33)	0.692	AGE (p=0.006) RACE (p=0.101)
6[d]	889	1.07 (0.83,1.38)	0.604	AGE (p=0.006) RACE (p=0.095)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

C.I.=[0.25,0.94]). Ranch Hands were half as likely as Comparisons to have abnormal patellar reflexes (1.3% vs. 2.6%). Stratifying the unadjusted analysis by occupation revealed a significant group difference within the officer stratum (p=0.033, Est. RR=0.25, 95% C.I.=[0.07,0.86]), in which the percentage of patellar reflex abnormalities was lower for the Ranch Hands than for the Comparisons (0.8% vs. 3.2%). In the enlisted flyer stratum, the relative risk was less than 1.00 but not significant (p=0.137, Est. RR=0.17); in the enlisted groundcrew stratum, the relative risk was greater than 1.00 but not significant (p=0.999, Est. RR=1.10).

The adjusted Model 1 analysis contained a significant interaction between group and lifetime alcohol history (Table 11-24(b): $p<0.001$). Appendix Table G-2-8 presents adjusted results stratified by lifetime alcohol history. In addition to this interaction, the final model included age and three covariate-by-covariate interactions: occupation-by-lifetime alcohol history, lifetime alcohol history-by-diabetic class, and insecticide exposure-by-diabetic class. After the group-by-lifetime alcohol history interaction was removed, the adjusted analysis detected a significant overall group difference (Table 11-24(b): p=0.009, Adj. RR=0.40, 95% C.I.=[0.19,0.83]). Stratifying the adjusted analysis by occupation revealed significantly fewer abnormalities for Ranch Hands relative to Comparisons within the officer and enlisted flyer strata (p=0.021, Adj. RR=0.21, 95% C.I.=[0.06,0.79] and p=0.048, Adj. RR=0.05, 95% C.I.=[0.00,0.98] for officers and enlisted flyers respectively).

The unadjusted and adjusted Model 2 results did not reveal a significant association between initial dioxin and patellar reflex (Table 11-24(c,d): $p>0.51$ for both analyses). The final adjusted model contained age, lifetime alcohol history, and diabetic class.

For Model 3, the unadjusted analysis of patellar reflex showed a significant contrast between background Ranch Hands and Comparisons (Table 11-24(e): p=0.033, Est. RR=0.11, 95% C.I.=[0.02,0.84]). Background Ranch Hands were considerably less likely than Comparisons to have abnormal patellar reflexes (0.3% vs. 2.7%). There were fewer abnormalities in the low, high, and low plus high Ranch Hand categories (1.9% in each) than in the Comparison group, but the estimated relative risks were not significant ($p>0.30$).

Categorized dioxin-by-lifetime alcohol history was a significant interaction in the adjusted Model 3 analysis of patellar reflex. Appendix Table G-2-8 presents adjusted results stratified by lifetime alcohol history categories. The adjusted analysis also included age, diabetic class, and an occupation-by-lifetime alcohol history interaction. Without the categorized dioxin-by-lifetime alcohol history interaction, the adjusted analysis detected a relative risk significantly less than 1.00 for the background Ranch Hands (Table 11-24(f): p=0.025, Adj. RR=0.09, 95% C.I.=[0.01,0.75]) and a relative risk marginally less than 1.00 for the low Ranch Hands (p=0.098, Adj. RR=0.38, 95% C.I.=[0.12,1.19]). When occupation and diabetic class were removed from the final model, the relative risk for the low Ranch Hands became nonsignificant (Appendix Table G-3-9(b): p=0.187.

The unadjusted analyses for Models 4 through 6 did not reveal a significant association between current dioxin and patellar reflex (Table 11-24(g): $p>0.13$ for each analysis). By contrast, the adjusted analyses for Models 4 and 5 detected a marginally significant positive

Table 11-24.
Analysis of Patellar Reflex

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***946***	***1.3***	***0.48 (0.25,0.94)***	***0.043***
	Comparison	***1,276***	***2.6***		
Officer	Ranch Hand	366	0.8	0.25 (0.07,0.86)	0.033
	Comparison	499	3.2		
Enlisted Flyer	Ranch Hand	162	0.6	0.17 (0.02,1.41)	0.137
	Comparison	201	3.5		
Enlisted Groundcrew	Ranch Hand	418	1.9	1.10 (0.43,2.82)	0.999
	Comparison	576	1.7		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***0.40 (0.19,0.83)*****	***0.009*****	GROUP*DRKYR (p<0.001) AGE (p<0.001) OCC*DRKYR (p=0.001) DRKYR*DIAB (p=0.026) INS*DIAB (p=0.016)
Officer	0.21 (0.06,0.79)**	0.021**	
Enlisted Flyer	0.05 (0.00,0.98)**	0.048**	
Enlisted Groundcrew	1.10 (0.40,2.99)**	0.854**	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interaction ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table G-2-8 for further analysis of this interaction.

Table 11-24. (Continued)
Analysis of Patellar Reflex

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	174	1.7	0.93 (0.58,1.48)	0.756
Medium	173	2.3		
High	170	1.8		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
504	1.19 (0.71,2.02)	0.516	AGE (p=0.028) DRKYR (p=0.056) DIAB (p=0.132)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 11-24. (Continued)
Analysis of Patellar Reflex

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,059	2.7		
Background RH	371	0.3	0.11 (0.02,0.84)	0.033
Low RH	260	1.9	0.62 (0.24,1.63)	0.334
High RH	257	1.9	0.60 (0.23,1.58)	0.301
Low plus High RH	517	1.9	0.61 (0.29,1.27)	0.188

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,040			DXCAT*DRKYR (p=0.002) AGE (p=0.002) DIAB (p<0.001) OCC*DRKYR (p<0.001)
Background RH	363	0.09 (0.01,0.75)**	0.025**	
Low RH	254	0.38 (0.12,1.19)**	0.098**	
High RH	250	0.81 (0.29,2.28)**	0.688**	
Low plus High RH	504	0.55 (0.25,1.22)**	0.143**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table G-2-8 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 11-24. (Continued)
Analysis of Patellar Reflex

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	0.3 (293)	1.0 (299)	2.4 (296)	1.29 (0.88,1.88)	0.204
5	0.3 (298)	2.0 (296)	1.4 (294)	1.21 (0.86,1.71)	0.275
6[c]	0.3 (297)	2.0 (296)	1.4 (294)	1.33 (0.92,1.92)	0.138

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	867	1.55 (0.99,2.41)	0.058	DRKYR (p=0.029) DIAB (p=0.082) AGE (p=0.019)
5	867	1.41 (0.94,2.12)	0.098	AGE (p=0.023) DRKYR (p=0.030) DIAB (p=0.084)
6[d]	866	1.58 (1.03,2.45)	0.039	AGE (p=0.021) DRKYR (p=0.034) DIAB (p=0.077)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

association between current dioxin and patellar reflex (Table 11-24(h): p=0.058, Adj. RR=1.55, 95% C.I.=[0.99,2.41] and p=0.098, Adj. RR=1.41, 95% C.I.=[0.94,2.12] for Models 4 and 5 respectively). The adjusted Model 6 analysis revealed a significant positive association between current dioxin and patellar reflex (Table 11-24(h): p=0.039, Adj. RR=1.58, 95% C.I.=[1.03,2.45]). Each of the adjusted analyses for Models 4 through 6 contained age, lifetime alcohol history, and diabetic class. For Model 4, the adjusted results changed slightly when diabetic class was removed from the final model. Without diabetic class, the relative risk became significant (Appendix Table G-3-9(c): p=0.050, Adj. RR=1.56, 95% C.I.=[1.01,2.41]).

Achilles Reflex

The unadjusted and adjusted Model 1 analyses did not reveal significant differences between the Ranch Hands and Comparisons in the percentage of Achilles reflex abnormalities (Table 11-25(a,b): $p > 0.25$ for all contrasts). The adjusted analysis included age, diabetic class, and an occupation-by-lifetime alcohol history interaction.

The Model 2 unadjusted results did not show a significant association between initial dioxin and Achilles reflex (Table 11-25(c): p=0.634). Initial dioxin-by-lifetime alcohol history was a significant interaction (p=0.030) in the adjusted Model 2 analysis. Appendix Table G-2-9 presents adjusted results stratified by lifetime alcohol history categories. The adjusted model also included age, insecticide exposure, and diabetic class. When the initial dioxin-by-lifetime alcohol history interaction was removed from the final model, the adjusted analysis did not reveal a significant association between initial dioxin and Achilles reflex (Table 11-25(d): p=0.612).

The unadjusted Model 3 analysis of Achilles reflex did not show any of the Ranch Hand categories to differ significantly with the Comparison group (Table 11-25(e): $p > 0.35$ for all contrasts). The adjusted Model 3 analysis contained a significant interaction between categorized dioxin and lifetime alcohol history (Table 11-25(f): p=0.006). Appendix Table G-2-9 displays adjusted results stratified by lifetime alcohol history categories. In addition to the categorized dioxin-by-lifetime alcohol history interaction, the adjusted analysis included diabetic class and an age-by-lifetime alcohol history interaction. The adjusted analysis did not reveal a significant contrast involving Comparisons when the categorized dioxin-by-lifetime alcohol history interaction was removed from the final model (Table 11-25(f): $p > 0.60$ for all contrasts).

For Models 4 through 6, the unadjusted and adjusted analyses did not reveal a significant association between current dioxin and Achilles reflex (Table 11-25(g,h): $p > 0.41$ for all analyses). Each of the adjusted analyses contained age, diabetic class, and an occupation-by-lifetime alcohol history interaction.

Table 11-25.
Analysis of Achilles Reflex

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***944***	***10.0***	***1.11 (0.83,1.48)***	***0.519***
	Comparison	***1,270***	***9.1***		
Officer	Ranch Hand	365	12.1	1.32 (0.85,2.04)	0.257
	Comparison	499	9.4		
Enlisted Flyer	Ranch Hand	162	9.9	0.93 (0.47,1.85)	0.971
	Comparison	199	10.6		
Enlisted Groundcrew	Ranch Hand	417	8.2	0.99 (0.63,1.57)	0.999
	Comparison	572	8.2		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.05 (0.78,1.41)***	***0.767***	AGE ($p<0.001$)
Officer	1.18 (0.75,1.86)	0.486	DIAB ($p<0.001$)
Enlisted Flyer	0.95 (0.47,1.93)	0.893	OCC*DRKYR ($p=0.040$)
Enlisted Groundcrew	0.96 (0.59,1.56)	0.868	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 11-25. (Continued)
Analysis of Achilles Reflex

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	173	11.6	0.95 (0.77,1.18)	0.634
Medium	173	11.0		
High	170	8.8		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
503	1.06 (0.84,1.34)**	0.612**	INIT*DRKYR (p=0.030) AGE (p=0.063) INS (p=0.075) DIAB (p=0.039)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table G-2-9 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 11-25. (Continued)
Analysis of Achilles Reflex

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,059	9.1		
Background RH	371	9.2	1.10 (0.73,1.67)	0.638
Low RH	259	11.6	1.23 (0.79,1.91)	0.352
High RH	257	9.3	0.96 (0.60,1.55)	0.879
Low plus High RH	516	10.5	1.10 (0.77,1.56)	0.610

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,040			DXCAT*DRKYR (p=0.006) DIAB (p<0.001) AGE*DRKYR (p=0.009)
Background RH	363	1.05 (0.68,1.62)**	0.825**	
Low RH	253	1.01 (0.63,1.61)**	0.972**	
High RH	250	1.11 (0.68,1.81)**	0.684**	
Low plus High RH	503	1.10 (0.76,1.59)**	0.603**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table G-2-9 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 11-25. (Continued)
Analysis of Achilles Reflex

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Abnormal/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	8.9 (293)	10.7 (298)	10.1 (296)	1.02 (0.88,1.18)	0.804
5	8.1 (298)	11.2 (295)	10.5 (294)	1.02 (0.90,1.16)	0.744
6[c]	8.1 (297)	11.2 (295)	10.5 (294)	1.00 (0.87,1.15)	0.974

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	866	1.08 (0.89,1.32)	0.411	AGE (p<0.001) DIAB (p=0.041) OCC*DRKYR (p=0.031)
5	866	1.06 (0.90,1.25)	0.487	AGE (p<0.001) DIAB (p=0.041) OCC*DRKYR (p=0.031)
6[d]	865	1.06 (0.89,1.27)	0.515	AGE (p<0.001) DIAB (p=0.041) OCC*DRKYR (p=0.031)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Biceps Reflex

The unadjusted and adjusted Model 1 analyses of biceps reflex did not show the Ranch Hands and Comparisons to differ significantly (Table 11-26(a,b): $p>0.31$ for all contrasts). The estimated and adjusted relative risks for the enlisted flyers were not calculated because no enlisted flyer Ranch Hands had abnormalities. The final adjusted model contained age and diabetic class.

For Model 2, the unadjusted analysis detected a significant inverse association between initial dioxin and biceps reflex (Table 11-26(c): $p=0.030$, Est. RR=0.47, 95% C.I.=[0.21,1.06]). After adjusting for occupation, the association between initial dioxin and biceps reflex became nonsignificant (Table 11-26(d): $p=0.389$).

In the unadjusted and adjusted Model 3 analyses, the prevalence of biceps reflex abnormalities did not differ significantly between any of the Ranch Hand categories and the Comparison group (Table 11-26(e,f): $p>0.17$ for all contrasts). Relative risks were not calculated for the background Ranch Hand versus Comparison contrast because there were no background Ranch Hands with abnormalities. The adjusted analysis contained the covariate age.

The unadjusted analyses for Models 4 through 6 did not reveal a significant association between current dioxin and biceps reflex (Table 11-26(g): $p>0.45$ for all analyses). The adjusted analyses for Models 4 and 5 were not significant although the adjusted relative risks for a twofold increase in current dioxin exceeded 1.4 in both final models (Table 11-26(h): $p=0.115$, Adj. RR=1.76, 95% C.I.=[0.87,3.55] and $p=0.245$, Adj. RR=1.43, 95% C.I.=[0.78,2.65]). The adjusted Model 6 analysis, which forced total lipids into the model, found a marginally significant positive association between whole-weight current dioxin and biceps reflex (Table 11-26(h): $p=0.059$, Adj. RR=1.98, 95% C.I.=[0.95,4.14]). Age and occupation were significant covariates in each of the adjusted models. Removing occupation from the adjusted Model 6 analysis caused the association between current dioxin and biceps reflex to become nonsignificant (Appendix Table G-3-11(a): $p=0.243$).

Babinski Reflex

The unadjusted and adjusted Model 1 analyses did not find a significant group difference in the percentage of Babinski reflex abnormalities (Table 11-27(a,b): $p>0.36$ for all contrasts). Relative risks for the officer and enlisted flyer categories were not calculated because there were no Ranch Hands with abnormalities in either of these strata. The final adjusted model contained age and insecticide exposure.

Statistical analyses for Model 2 were not conducted because there was only one Ranch Hand in the Model 2 analysis with an abnormal Babinski reflex. This participant was in the low initial dioxin category. Table 11-27(c) displays percentages of abnormalities by initial dioxin category.

The unadjusted and adjusted Model 3 analyses of Babinski reflex did not find a significant difference between any of the Ranch Hand categories and the Comparison group

Table 11-26.
Analysis of Biceps Reflex

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***948***	***0.7***	***0.67 (0.27,1.67)***	***0.524***
	Comparison	***1,280***	***1.1***		
Officer	Ranch Hand	367	1.4	1.14 (0.35,3.76)	0.999
	Comparison	501	1.2		
Enlisted Flyer	Ranch Hand	162	0.0	--	0.580
	Comparison	203	1.0		
Enlisted Groundcrew	Ranch Hand	419	0.5	0.46 (0.09,2.27)	0.532
	Comparison	576	1.0		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***0.64 (0.26,1.60)***	***0.332***	AGE (p=0.007) DIAB (p=0.109)
Officer	1.05 (0.32,3.51)	0.932	
Enlisted Flyer	--	--	
Enlisted Groundcrew	0.44 (0.09,2.21)	0.319	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

--: Relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

Table 11-26. (Continued)
Analysis of Biceps Reflex

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	174	2.3	0.47 (0.21,1.06)	0.030
Medium	173	1.7		
High	170	0.0		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
517	0.69 (0.29,1.66)	0.389	OCC (p=0.081)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 11-26. (Continued)
Analysis of Biceps Reflex

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,062	1.2		
Background RH	373	0.0	--	0.584
Low RH	260	2.3	1.60 (0.59,4.33)	0.351
High RH	257	0.4	0.24 (0.03,1.89)	0.174
Low plus High RH	517	1.4	0.91 (0.35,2.34)	0.837

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,062			AGE (p=0.016)
Background RH	373	--	--	
Low RH	260	1.42 (0.52,3.90)	0.492	
High RH	257	0.30 (0.04,2.36)	0.251	
Low plus High RH	517	0.93 (0.36,2.43)	0.885	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

--: Relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 11-26. (Continued)
Analysis of Biceps Reflex

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	0.0 (294)	1.3 (300)	1.0 (296)	1.10 (0.67,1.81)	0.704
5	0.0 (299)	2.0 (297)	0.3 (294)	1.04 (0.67,1.61)	0.871
6[c]	0.0 (298)	2.0 (297)	0.3 (294)	1.20 (0.75,1.92)	0.459

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	890	1.76 (0.87,3.55)	0.115	AGE (p=0.043) OCC (p=0.092)
5	890	1.43 (0.78,2.65)	0.245	AGE (p=0.044) OCC (p=0.133)
6[d]	889	1.98 (0.95,4.14)	0.059	AGE (p=0.035) OCC (p=0.088)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 11-27.
Analysis of Babinski Reflex

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***948***	***0.3***	***0.50 (0.13,1.91)***	***0.469***
	Comparison	***1,278***	***0.6***		
Officer	Ranch Hand	367	0.0	--	0.367
	Comparison	500	0.6		
Enlisted Flyer	Ranch Hand	162	0.0	--	0.578
	Comparison	202	1.0		
Enlisted Groundcrew	Ranch Hand	419	0.7	1.38 (0.28,6.86)	0.999
	Comparison	576	0.5		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***0.57 (0.15,2.17)***	***0.388***	AGE (p=0.035) INS (p=0.121)
Officer	--	--	
Enlisted Flyer	--	--	
Enlisted Groundcrew	1.52 (0.30,7.67)	0.614	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

--: Relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

Table 11-27. (Continued)
Analysis of Babinski Reflex

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)	p-Value
Low	174	0.6	--	--
Medium	173	0.0		
High	170	0.0		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)			
n	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
--	--	--	--

--: Analysis not conducted due to the sparse number of abnormalities.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 11-27. (Continued)
Analysis of Babinski Reflex

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,061	0.7		
Background RH	373	0.5	0.72 (0.15,3.53)	0.684
Low RH	260	0.4	0.55 (0.07,4.54)	0.578
High RH	257	0.0	--	0.408
Low plus High RH	517	0.2	0.28 (0.03,2.37)	0.244

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,061			AGE (p=0.016) OCC (p=0.097)
Background RH	373	0.83 (0.16,4.33)	0.826	
Low RH	260	0.52 (0.06,4.43)	0.552	
High RH	257	--	--	
Low plus High RH	517	0.25 (0.03,2.13)	0.206	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

--: Relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 11-27. (Continued)
Analysis of Babinski Reflex

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	0.7 (294)	0.3 (300)	0.0 (296)	0.47 (0.20,1.13)	0.087
5	0.7 (299)	0.3 (297)	0.0 (294)	0.64 (0.38,1.08)	0.131
6[c]	0.7 (298)	0.3 (297)	0.0 (294)	0.63 (0.36,1.11)	0.154

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	890	0.43 (0.19,0.98)	0.039	AGE (p=0.086) OCC (p=0.014)
5	890	0.59 (0.35,0.98)	0.062	AGE (p=0.073) OCC (p=0.015)
6[d]	889	0.60 (0.34,1.05)	0.092	AGE (p=0.072) OCC (p=0.016)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

(Table 11-27(e,f): $p>0.20$ for all contrasts). Relative risks for the high Ranch Hand contrast were not computed because there were no abnormalities in the high Ranch Hand category. The adjusted analysis contained age and occupation.

For Model 4, the unadjusted analysis revealed a marginally significant inverse association between lipid-adjusted current dioxin and Babinski reflex (Table 11-27(g): $p=0.087$, Est. RR=0.47, 95% C.I.=[0.20,1.13]). The unadjusted analyses for Models 5 and 6 did not find a significant association (Table 11-27(g): $p>0.13$ for both contrasts).

In the adjusted analyses, the association between current dioxin and Babinski reflex became significant for Model 4 and marginally significant for Models 5 and 6 (Table 11-27(h): $p=0.039$, Adj. RR=0.43, 95% C.I.=[0.19,0.98]; $p=0.062$, Adj. RR=0.59, 95% C.I.=[0.35,0.98]; and $p=0.092$, Adj. RR=0.60, 95% C.I.=[0.34,1.05] respectively). Age and occupation were significant in each adjusted model. The associations became nonsignificant in Models 4 through 6 when occupation was removed from each of the adjusted analyses (Appendix Table G-3-12(b): $p>0.10$ in each model).

Vibrotactile Threshold Measurement of Right Great Toe

The unadjusted and adjusted Model 1 analyses for vibrotactile threshold measurement of the right great toe did not find a significant difference between Ranch Hands and Comparisons (Table 11-28(a,b): $p>0.13$ for all contrasts). The final adjusted model contained age, occupation, and an insecticide exposure-by-diabetic class interaction.

For Model 2, the unadjusted analysis did not reveal a significant association between initial dioxin and vibrotactile threshold measurement of the right great toe (Table 11-28(c): $p=0.218$). The adjusted analysis contained an initial dioxin-by-composite exposure to heavy metals interaction (Table 11-28(d): $p=0.002$). Appendix Table G-2-10 presents adjusted results stratified by composite exposure to heavy metals. In addition to this interaction, the adjusted analysis included age, lifetime alcohol history, and an occupation-by-worked with vibrating power equipment or tools interaction. The adjusted analysis did not reveal a significant association between initial dioxin and vibrotactile threshold measurement of the right great toe when the initial dioxin-by-composite exposure to heavy metals interaction was removed from the final model ($p=0.438$).

The unadjusted Model 3 analysis of vibrotacitle threshold measurement of the right great toe did not reveal a significant contrast between any of the Ranch Hand categories and the Comparison group (Table 11-28(e): $p>0.38$ for all contrasts). The adjusted Model 3 analysis retained a categorized dioxin-by-lifetime alcohol history interaction (Table 11-28(f): $p<0.001$). Appendix Table G-2-10 displays adjusted results stratified by lifetime alcohol history categories. The adjusted analysis also included the covariate age and three covariate-by-covariate interactions: lifetime alcohol history-by-occupation, insecticide exposure-by-diabetic class, and diabetic class-by-composite exposure to heavy metals. After removing the categorized dioxin-by-lifetime alcohol history interaction, the adjusted analysis did not show any of the Ranch Hand categories to be significantly different from the Comparison group (Table 11-28(f): $p>0.26$ for all contrasts).

Table 11-28.
Analysis of Vibrotactile Threshold Measurement of Right Great Toe (microns)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***946***	***16.66***	***0.04--***	***0.957***
	Comparison	***1,277***	***16.61***		
Officer	Ranch Hand	366	16.97	-1.48--	0.303
	Comparison	499	18.45		
Enlisted Flyer	Ranch Hand	162	20.18	0.88--	0.711
	Comparison	203	19.29		
Enlisted Groundcrew	Ranch Hand	418	15.21	0.83--	0.442
	Comparison	575	14.38		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]	Covariate Remarks[d]
All	***Ranch Hand***	***945***	***16.28***	***-0.19--***	0.798	AGE ($p<0.001$)
	Comparison	***1,275***	***16.48***			OCC ($p<0.001$)
Officer	Ranch Hand	366	13.32	-1.54--	0.136	INS*DIAB ($p=0.012$)
	Comparison	499	14.86			
Enlisted Flyer	Ranch Hand	162	17.46	0.23--	0.904	
	Comparison	202	17.22			
Enlisted Groundcrew	Ranch Hand	417	18.62	1.16--	0.349	
	Comparison	574	17.46			

[a] Transformed from the natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 11-28. (Continued)
Analysis of Vibrotactile Threshold Measurement of Right Great Toe (microns)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	173	17.18	17.06	0.002	-0.0473 (0.0384)	0.218
Medium	172	21.11	21.21			
High	170	14.73	14.77			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	171	17.43**	0.165	0.0325 (0.0419)**	0.438**	INIT*HVMET (p=0.002) AGE (p<0.001) DRKYR (p=0.057) OCC*PWTOOL (p=0.016)
Medium	167	23.20**				
High	165	19.06**				

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on natural logarithm of vibrotactile threshold measurement of right great toe versus log_2 (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table G-2-10 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 11-28. (Continued)
Analysis of Vibrotactile Threshold Measurement of Right Great Toe (microns)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,059	17.05	17.05		
Background RH	373	15.98	16.47	-0.58--	0.620
Low RH	258	18.73	18.27	1.22--	0.384
High RH	257	16.33	16.03	-1.02--	0.438
Low plus High RH	515	17.49	17.11	0.06--	0.953

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Mean[ae]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	1,040	17.35**			DXCAT*DRKYR (p<0.001) AGE (p<0.001) DRKYR*OCC (p=0.040) INS*DIAB (p=0.024) DIAB*HVMET (p=0.018)
Background RH	365	16.11**	-1.24--**	0.266**	
Low RH	253	17.13**	-0.22--**	0.864**	
High RH	250	18.40**	1.05--**	0.448**	
Low plus High RH	503	17.76**	0.40--**	0.696**	

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($p \leq 0.05$); adjusted mean, difference of adjusted means, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table G-2-10 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 11-28. (Continued)
Analysis of Vibrotactile Threshold Measurement of Right Great Toe (microns)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[b]	Current Dioxin Category Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Slope (Std. Error)[c]	p-Value
4	14.96 (294)	19.34 (299)	16.47 (295)	<0.001	0.0017 (0.0271)	0.950
5	14.93 (299)	19.32 (295)	16.59 (294)	<0.001	0.0067 (0.0232)	0.772
6[d]	15.25 (298)	19.35 (295)	16.27 (294)	0.002	-0.0082 (0.0251)	0.744

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[b]	Current Dioxin Category Adjusted Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	15.42** (290)	18.41** (292)	18.36** (286)	0.171	0.0290 (0.0295)**	0.326**	CURR*DRKYR (p=0.001) CURR*HVMET (p=0.003) AGE (p<0.001) OCC (p=0.025) DIAB*PWTOOL (p=0.041)
5	15.25** (294)	18.66** (289)	18.08** (285)	0.169	0.0243 (0.0249)**	0.328**	CURR*DRKYR (p=0.002) CURR*HVMET (p=0.012) AGE (p<0.001) OCC (p=0.028) DIAB*PWTOOL (p=0.045)
6[e]	15.40** (293)	18.73** (289)	18.17** (285)	0.168	0.0178 (0.0269)**	0.508**	CURR*DRKYR (p=0.002) CURR*HVMET (p=0.027) AGE (p<0.001) OCC (p=0.027) DIAB*PWTOOL (p=0.046)

[a] Transformed from natural logarithm scale.

[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[c] Slope and standard error based on natural logarithm of vibrotactile threshold measurement of right great toe versus log_2 (current dioxin + 1).

[d] Adjusted for log_2 total lipids.

[e] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interactions ($p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table G-2-10 for further analysis of these interactions.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

The unadjusted analyses for Models 4 through 6 did not reveal a significant association between current dioxin and vibrotactile threshold measurement of the right great toe (Table 11-28(g): $p>0.74$ for all analyses). Each of the adjusted analyses for Models 4 through 6 contained a current dioxin-by-lifetime alcohol history and a current dioxin-by-composite exposure to heavy metals interaction (Table 11-28(h): $p=0.001$ and $p=0.003$, $p=0.002$ and $p=0.012$, and $p=0.002$ and $p=0.027$ for Models 4, 5, and 6 respectively). Appendix Table G-2-10 displays adjusted results stratified separately by lifetime alcohol history and composite exposure to heavy metals for Models 4 through 6. In addition to these interactions, each of the adjusted analyses included age, occupation, and a diabetic class-by-worked with vibrating power equipment or tools interaction.

None of the adjusted analyses for Models 4 through 6 detected a significant association between current dioxin and vibrotactile threshold measurement of the right great toe when the current dioxin-by-lifetime alcohol history and current dioxin-by-composite exposure to heavy metals interactions were removed from each of the final models (Table 11-28(h): $p>0.32$ for each analysis). However, the association between current dioxin and vibrotactile threshold measurement of the right great toe became significant in Models 4 and 5 and marginally significant in Model 6 when occupation, diabetic class, and the current dioxin-by-covariate interactions were removed from the final models (Appendix Table G-3-13(c): $p=0.020$, Adj. Slope=0.0609; $p=0.025$, Adj. Slope=0.0498; and $p=0.056$, Adj. Slope=0.0463 for Models 4, 5, and 6).

Vibrotactile Threshold Measurement of Left Great Toe

The unadjusted and adjusted Model 1 analyses of vibrotactile threshold measurement of the left great toe did not find a significant difference between Ranch Hands and Comparisons (Table 11-29(a,b): $p>0.20$ for all contrasts). The final adjusted model contained age, race, occupation, and two covariate-by-covariate interactions: lifetime alcohol history-by-insecticide exposure and insecticide exposure-by-diabetic class.

For Model 2, the unadjusted analysis detected a marginally significant inverse association between initial dioxin and vibrotactile threshold measurement of the left great toe (Table 11-29(c): $p=0.061$, Est. Slope=-0.0720). An initial dioxin-by-diabetic class and an initial dioxin-by-composite exposure to heavy metals interaction were retained in the adjusted Model 2 analysis (Table 11-29(d): $p=0.033$ and $p=0.021$ respectively). Appendix Table G-2-11 presents adjusted results stratified separately by diabetic class and composite exposure to heavy metals. The adjusted analysis also included the covariates age, race, and worked with vibrating power equipment or tools. Without the initial dioxin-by-diabetic class and initial dioxin-by-composite exposure to heavy metals interactions, the adjusted analysis did not find a significant association between current dioxin and vibrotactile threshold measurement of the left great toe (Table 11-29(d): $p=0.833$).

The unadjusted and adjusted Model 3 analyses of vibrotactile threshold measurement of the left great toe did not reveal a significant contrast between any of the Ranch Hand categories and the Comparison group (Table 11-29(e,f): $p>0.18$ for all contrasts). The adjusted analysis contained age, race, occupation, and a lifetime alcohol history-by-insecticide exposure interaction.

Table 11-29.
Analysis of Vibrotactile Threshold Measurement of Left Great Toe (microns)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***946***	***17.12***	***0.70--***	***0.408***
	Comparison	***1,277***	***16.43***		
Officer	Ranch Hand	366	18.16	0.22--	0.880
	Comparison	500	17.94		
Enlisted Flyer	Ranch Hand	162	19.98	-0.39--	0.873
	Comparison	202	20.37		
Enlisted Groundcrew	Ranch Hand	418	15.32	1.21--	0.267
	Comparison	575	14.11		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]	Covariate Remarks[d]
All	***Ranch Hand***	***924***	***15.77***	***0.31--***	0.664	AGE ($p<0.001$)
	Comparison	***1,254***	***15.46***			RACE ($p=0.110$)
Officer	Ranch Hand	362	13.15	-0.25--	0.797	OCC ($p<0.001$)
	Comparison	492	13.40			DRKYR*INS ($p=0.016$)
Enlisted Flyer	Ranch Hand	156	15.90	-1.14--	0.540	INS*DIAB ($p=0.038$)
	Comparison	200	17.04			
Enlisted Groundcrew	Ranch Hand	406	18.09	1.52--	0.205	
	Comparison	562	16.58			

[a] Transformed from the natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 11-29. (Continued)
Analysis of Vibrotactile Threshold Measurement of Left Great Toe (microns)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	173	19.64	19.62	0.030	-0.0720 (0.0383)	0.061
Medium	172	18.74	18.94			
High	170	15.15	15.00			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	173	18.18**	0.194	0.0079 (0.0375)**	0.833**	INIT*DIAB (p=0.033) INIT*HVMET (p=0.021) AGE (p<0.001) RACE (p=0.112) PWTOOL (p=0.009)
Medium	172	19.18**				
High	170	18.08**				

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on natural logarithm of vibrotactile threshold measurement of left great toe versus log_2 (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interactions ($0.01 < p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table G-2-11 for further analysis of these interactions.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 11-29. (Continued)
Analysis of Vibrotactile Threshold Measurement of Left Great Toe (microns)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,060	16.93	16.93		
Background RH	373	16.66	17.24	0.31--	0.797
Low RH	258	19.39	18.80	1.87--	0.189
High RH	257	16.24	15.94	-0.99--	0.453
Low plus High RH	515	17.75	17.31	0.38--	0.719

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Mean[ac]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	1,042	15.71			AGE ($p<0.001$) RACE ($p=0.136$) OCC ($p<0.001$) DRKYR*INS ($p=0.012$)
Background RH	366	15.45	-0.26--	0.801	
Low RH	253	16.32	0.62--	0.603	
High RH	250	16.45	0.75--	0.545	
Low plus High RH	503	16.39	0.68--	0.466	

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 11-29. (Continued)
Analysis of Vibrotactile Threshold Measurement of Left Great Toe (microns)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[b]	Current Dioxin Category Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Slope (Std. Error)[c]	p-Value
4	15.85 (294)	20.05 (299)	16.20 (295)	<0.001	-0.0106 (0.0274)	0.698
5	15.82 (299)	19.62 (295)	16.64 (294)	<0.001	-0.0056 (0.0235)	0.813
6[d]	16.04 (298)	19.65 (295)	16.38 (294)	0.001	-0.0150 (0.0254)	0.557

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[b]	Current Dioxin Category Adjusted Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	17.08** (290)	19.92** (292)	19.08** (286)	0.207	0.0226 (0.0291)**	0.439**	CURR*DRKYR (p=0.004) CURR*DIAB (p=0.019) CURR*PWTOOL (p=0.005) AGE (p<0.001) OCC (p=0.046) HVMET (p=0.146)
5	16.63** (295)	19.32** (289)	18.88** (285)	0.200	0.0167 (0.0240)**	0.487**	CURR*DRKYR (p=0.002) CURR*PWTOOL (p=0.018) AGE (p<0.001) OCC (p=0.026) HVMET (p=0.133)
6[e]	16.52** (294)	19.29** (289)	19.04** (285)	0.200	0.0183 (0.0262)**	0.485**	CURR*DRKYR (p=0.002) CURR*PWTOOL (p=0.016) AGE (p<0.001) OCC (p=0.029) HVMET (p=0.145)

[a] Transformed from natural logarithm scale.

[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[c] Slope and standard error based on natural logarithm of vibrotactile threshold measurement of left great toe versus log_2 (current dioxin + 1).

[d] Adjusted for log_2 total lipids.

[e] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table G-2-11 for further analysis of these interactions.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

The unadjusted analyses for Models 4 through 6 did not reveal a significant association between current dioxin and vibrotactile threshold measurement of the left great toe (Table 11-29(g): $p > 0.55$ for each analysis). Each of the adjusted analyses for Models 4 through 6 contained a current dioxin-by-lifetime alcohol history and a current dioxin-by-worked with vibrating power equipment or tools interaction (Table 11-29(h): $p=0.004$ and $p=0.005$, $p=0.002$ and $p=0.018$, and $p=0.002$ and $p=0.016$ for Models 4, 5, and 6 respectively). Model 4 also contained a current dioxin-by-diabetic class interaction ($p=0.019$). Appendix Table G-2-11 presents adjusted results stratified separately by lifetime alcohol history and worked with vibrating power equipment or tools for Models 4 through 6. Appendix Table G-2-11 also displays adjusted results stratified by diabetic class for Model 4. In addition to these interactions, Models 4, 5, and 6 included age, occupation, and composite exposure to heavy metals.

None of the adjusted analyses for Models 4 through 6 found a significant association between current dioxin and vibrotactile threshold measurement of the left great toe when the current dioxin-by-covariate interactions were removed from each of the final models (Table 11-29(h): $p > 0.43$ for each analysis). However, the association between current dioxin and vibrotactile threshold measurement of the left great toe became significant in Model 4 and marginally significant in Models 5 and 6 after occupation, diabetic class, and the current dioxin-by-covariate interactions were removed from the adjusted analyses (Appendix Table G-3-14(c): $p=0.034$, Adj. Slope=0.0547; $p=0.054$, Adj. Slope=0.0422; and $p=0.057$, Adj. Slope=0.0454 for Models 4, 5, and 6 respectively).

Physical Examination Variables: CNS Coordination Processes

Tremor

The unadjusted and adjusted Model 1 analyses of tremor did not find a significant difference between Ranch Hands and Comparisons (Table 11-30(a,b): $p > 0.10$ for all contrasts). The adjusted analysis contained an age-by-lifetime alcohol history interaction.

Additional unadjusted and adjusted Model 1 analyses for tremor were conducted with the enlisted flyers and enlisted groundcrew combined into one stratum. This unadjusted analysis found a marginally significant group difference within the enlisted stratum (Appendix Table G-5-3(a): $p=0.081$, Est. RR=1.95, 95% C.I.=[0.98, 3.89]). Among enlisted participants, the percentage of abnormalities was higher for the Ranch Hands than for the Comparisons (Table G-5-3(a): 3.4% versus 1.8%). The adjusted analyses combining enlisted flyers and enlisted groundcrew did not detect a significant overall group difference (Appendix Table G-5-3(b): $p=0.755$). For the enlisted participants, the relative risk remained marginally significant (Appendix Table G-5-3(b): $p=0.094$, Adj. RR=1.83, 95% C.I.=[0.90, 3.69]). The group-by-age and age-by-lifetime alcohol history interactions were retained in this adjusted analysis.

The unadjusted and adjusted results for Model 2 did not show a significant association between initial dioxin and tremor (Table 11-30(c,d): $p > 0.12$ for both analyses). The final model included an age-by-occupation interaction.

Table 11-30.
Analysis of Tremor

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***948***	***3.0***	***1.12 (0.67,1.85)***	***0.771***
	Comparison	***1,280***	***2.7***		
Officer	Ranch Hand	367	2.2	0.54 (0.23,1.23)	0.194
	Comparison	501	4.0		
Enlisted Flyer	Ranch Hand	162	3.7	3.87 (0.77,19.41)	0.161
	Comparison	203	1.0		
Enlisted Groundcrew	Ranch Hand	419	3.3	1.63 (0.74,3.55)	0.304
	Comparison	576	2.1		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.09 (0.65,1.83)***	***0.754***	AGE*DRKYR (p=0.036)
Officer	0.55 (0.24,1.28)	0.166	
Enlisted Flyer	3.84 (0.76,19.35)	0.104	
Enlisted Groundcrew	1.49 (0.67,3.33)	0.332	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 11-30. (Continued)
Analysis of Tremor

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent Abnormal**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	174	1.1	1.28 (0.85,1.94)	0.244
Medium	173	2.9		
High	170	3.5		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**	**Covariate Remarks**
517	1.47 (0.90,2.40)	0.129	AGE*OCC (p=0.011)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 11-30. (Continued)
Analysis of Tremor

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,062	2.7		
Background RH	373	3.2	1.19 (0.60,2.37)	0.623
Low RH	260	1.5	0.57 (0.20,1.62)	0.289
High RH	257	3.5	1.27 (0.59,2.73)	0.539
Low plus High RH	517	2.5	0.92 (0.47,1.78)	0.797

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,044			AGE (p=0.043) DRKYR (p=0.145)
Background RH	366	1.16 (0.58,2.33)	0.674	
Low RH	254	0.57 (0.20,1.65)	0.303	
High RH	250	1.30 (0.58,2.93)	0.530	
Low plus High RH	504	0.91 (0.46,1.81)	0.785	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 11-30. (Continued)
Analysis of Tremor

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Abnormal/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	3.7 (294)	1.0 (300)	3.7 (296)	0.97 (0.73,1.28)	0.819
5	3.0 (299)	2.0 (297)	3.4 (294)	0.98 (0.78,1.24)	0.898
6[c]	3.0 (298)	2.0 (297)	3.4 (294)	0.96 (0.75,1.24)	0.750

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	869	0.95 (0.70,1.29)**	0.735**	CURR*AGE (p=0.009) DIAB*DRKYR (p=0.037)
5	890	0.98 (0.78,1.24)	0.898	
6[d]	889	0.96 (0.75,1.24)	0.750	

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table G-2-12 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

For Model 3, the unadjusted and adjusted analyses of tremor did not reveal any of the Ranch Hand categories to be significantly different from the Comparison group (Table 11-30(e,f): $p > 0.28$ for all contrasts). Age and lifetime alcohol history were retained in the final model.

The unadjusted analyses of Models 4 through 6 did not reveal a significant association between current dioxin and tremor (Table 11-30(g): $p \geq 0.75$ for all analyses). Current dioxin-by-age was a significant interaction in the adjusted analysis of Model 4 (Table 11-30(h): $p = 0.009$). Appendix Table G-2-12 presents adjusted results stratified by age. In addition to the current dioxin-by-age interaction, the adjusted model included a diabetic class-by-lifetime alcohol history interaction. The adjusted Model 4 analysis did not find a significant association between current dioxin and tremor after the current dioxin-by-age interaction was removed from the final model (Table 11-30(h): $p = 0.735$). For Models 5 and 6, the unadjusted and adjusted results were identical because no covariates were retained in the final model.

Coordination

The unadjusted and adjusted Model 1 analyses did not reveal a significant group difference in the percentage of coordination abnormalities (Table 11-31(a,b): $p > 0.25$ for all contrasts). Age was retained in the final adjusted model.

For Model 2, the unadjusted and adjusted analyses did not reveal a significant association between initial dioxin and coordination (Table 11-31(c,d): $p > 0.62$ for both analyses). The final model contained the covariate age.

The unadjusted and adjusted results for Model 3 did not show a significant difference in the percentage of coordination abnormalities between any of the Ranch Hand categories and the Comparison group (Table 11-31(e,f): $p > 0.47$ for all contrasts). Age was significant in the adjusted analysis.

The unadjusted and adjusted analyses for Models 4 through 6 did not reveal a significant association between current dioxin and coordination (Table 11-31(g,h): $p > 0.72$ for all analyses). Each of the adjusted analyses for Models 4 through 6 contained age.

Romberg Sign

For Model 1, the unadjusted and adjusted analyses did not show a significant group difference in the percentage of Romberg sign abnormalities (Table 11-32(a,b): $p > 0.24$ for all contrasts). Relative risks were not estimated for the enlisted flyer stratum because no enlisted flyer Ranch Hand had an abnormal Romerg sign. The final adjusted model contained the covariates age and diabetic class.

The unadjusted and adjusted Model 2 analyses did not reveal a significant association between initial dioxin and Romberg sign (Table 11-32(c,d): $p > 0.41$ for both analyses). Age was retained in the adjusted analysis.

Table 11-31.
Analysis of Coordination

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***947***	***2.2***	***1.14 (0.63,2.04)***	***0.781***
	Comparison	***1,278***	***2.0***		
Officer	Ranch Hand	366	2.2	1.00 (0.40,2.50)	0.999
	Comparison	501	2.2		
Enlisted Flyer	Ranch Hand	162	1.2	0.49 (0.09,2.56)	0.632
	Comparison	201	2.5		
Enlisted Groundcrew	Ranch Hand	419	2.6	1.70 (0.70,4.14)	0.342
	Comparison	576	1.6		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.13 (0.62,2.03)***	***0.695***	AGE ($p < 0.001$)
Officer	1.00 (0.40,2.53)	0.999	
Enlisted Flyer	0.47 (0.09,2.48)	0.374	
Enlisted Groundcrew	1.70 (0.69,4.19)	0.251	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 11-31. (Continued)
Analysis of Coordination

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent Abnormal**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	174	2.3	0.90 (0.58,1.39)	0.622
Medium	172	2.9		
High	170	2.4		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**	**Covariate Remarks**
516	1.02 (0.65,1.61)	0.918	AGE (p=0.023)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 11-31. (Continued)
Analysis of Coordination

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,062	2.2		
Background RH	373	1.9	0.83 (0.35,1.96)	0.664
Low RH	259	2.7	1.20 (0.51,2.84)	0.681
High RH	257	2.3	1.09 (0.43,2.74)	0.858
Low plus High RH	516	2.5	1.15 (0.57,2.30)	0.703

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,062			AGE ($p<0.001$)
Background RH	373	0.75 (0.31,1.79)	0.516	
Low RH	259	1.12 (0.47,2.69)	0.797	
High RH	257	1.41 (0.55,3.58)	0.475	
Low plus High RH	516	1.24 (0.61,2.50)	0.556	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 11-31. (Continued)
Analysis of Coordination

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	2.0 (294)	2.0 (300)	2.7 (295)	0.97 (0.71,1.32)	0.829
5	1.7 (299)	2.4 (296)	2.7 (294)	0.99 (0.76,1.29)	0.949
6[c]	1.7 (298)	2.4 (296)	2.7 (294)	0.95 (0.72,1.26)	0.726

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	889	1.04 (0.75,1.45)	0.809	AGE (p=0.013)
5	889	1.05 (0.79,1.39)	0.734	AGE (p=0.012)
6[d]	888	1.02 (0.75,1.38)	0.919	AGE (p=0.014)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 11-32.
Analysis of Romberg Sign

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***947***	***0.5***	***1.13 (0.34,3.70)***	***0.999***
	Comparison	***1,279***	***0.5***		
Officer	Ranch Hand	366	0.5	1.37 (0.19,9.76)	0.999
	Comparison	500	0.4		
Enlisted Flyer	Ranch Hand	162	0.0	--	0.332
	Comparison	203	1.5		
Enlisted Groundcrew	Ranch Hand	419	0.7	4.15 (0.43,40.01)	0.408
	Comparison	576	0.2		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.03 (0.31,3.43)***	***0.960***	AGE (p=0.022) DIAB (p=0.006)
Officer	1.18 (0.16,8.55)	0.872	
Enlisted Flyer	--	--	
Enlisted Groundcrew	3.89 (0.40,38.26)	0.244	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

--: Relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

Table 11-32. (Continued)
Analysis of Romberg Sign

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	174	0.6	1.14 (0.51,2.51)	0.757
Medium	172	0.0		
High	170	1.2		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
516	1.42 (0.63,3.19)	0.414	AGE (p=0.059)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 11-32. (Continued)
Analysis of Romberg Sign

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,061	0.5		
Background RH	373	0.5	1.19 (0.23,6.29)	0.836
Low RH	259	0.4	0.71 (0.08,6.15)	0.755
High RH	257	0.8	1.31 (0.23,7.41)	0.760
Low plus High RH	516	0.6	1.01 (0.23,4.43)	0.994

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,061			AGE (p=0.023)
Background RH	373	1.10 (0.21,5.83)	0.912	
Low RH	259	0.61 (0.07,5.45)	0.662	
High RH	257	1.72 (0.31,9.61)	0.539	
Low plus High RH	516	1.06 (0.24,4.70)	0.935	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$ 10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin $\leq$ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 11-32. (Continued)
Analysis of Romberg Sign

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	0.3 (294)	0.7 (300)	0.7 (295)	1.08 (0.60,1.95)	0.788
5	0.3 (299)	0.3 (296)	1.0 (294)	1.10 (0.66,1.84)	0.717
6[c]	0.3 (298)	0.3 (296)	1.0 (294)	1.05 (0.60,1.83)	0.877

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	889	1.26 (0.66,2.42)	0.490	AGE (p=0.014)
5	889	1.25 (0.70,2.22)	0.455	AGE (p=0.013)
6[d]	888	1.20 (0.65,2.24)	0.565	AGE (p=0.014)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Displayed in Table 11-32(e,f), the unadjusted and adjusted Model 3 results did not reveal any of the Ranch Hand categories to be significantly different from the Comparison group in the percentage of Romberg sign abnormalities ($p > 0.53$ for all contrasts). The adjusted analysis contained the covariate age.

The unadjusted and adjusted results for Models 4 through 6 did not reveal a significant association between current dioxin and Romberg sign (Table 11-32(g,h): $p > 0.45$ for all analyses). Each of the adjusted analyses contained age.

Gait

The unadjusted and adjusted Model 1 analyses of gait did not show a significant group difference in percentage of gait abnormalities between Ranch Hands and Comparisons (Table 11-33(a,b): $p > 0.20$ for all contrasts). Age and lifetime alcohol history were significant covariates in the adjusted analysis.

For Model 2, the unadjusted analysis did not reveal a significant association between initial dioxin and gait (Table 11-33(c): $p = 0.598$). The interaction between initial dioxin and age was significant in the adjusted Model 2 analysis (Table 11-33(d): $p = 0.031$). Appendix Table G-2-13 displays adjusted results stratified by age. The final model also included an age-by-lifetime alcohol history interaction. Without the initial dioxin-by-age interaction, the adjusted analysis did not detect a significant association between initial dioxin and gait (Table 11-33(d): $p = 0.260$).

The unadjusted and adjusted analyses of gait for Model 3 did not reveal any of the Ranch Hand categories to be significantly different than the Comparison group (Table 11-33(e,f): $p > 0.18$ for all contrasts). The final model contained the covariates age and lifetime alcohol history.

The unadjusted and adjusted results for Models 4 through 6 did not reveal a significant association between current dioxin and gait (Table 11-33(g,h): $p > 0.66$ for all analyses). Each of the adjusted analyses contained age, occupation, and a diabetic class-by-insecticide exposure interaction.

Central Nervous System (CNS) Index

The unadjusted and adjusted Model 1 analyses of the CNS index did not reveal a significant difference between the Ranch Hands and Comparisons (Table 11-34(a,b): $p > 0.41$ for all contrasts). The adjusted model contained the covariates age, race, and lifetime alcohol history.

For Model 2, the unadjusted and adjusted analyses did not reveal a significant association between initial dioxin and the CNS index (Table 11-34(c,d): $p > 0.18$ for both analyses). Age was significant in the final model.

Table 11-33.
Analysis of Gait

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***948***	***3.5***	***1.12 (0.70,1.79)***	***0.732***
	Comparison	***1,279***	***3.1***		
Officer	Ranch Hand	367	2.7	0.91 (0.40,2.04)	0.973
	Comparison	500	3.0		
Enlisted Flyer	Ranch Hand	162	3.7	0.83 (0.29,2.38)	0.933
	Comparison	203	4.4		
Enlisted Groundcrew	Ranch Hand	419	4.1	1.48 (0.74,2.97)	0.351
	Comparison	576	2.8		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.14 (0.71,1.83)***	***0.597***	AGE (p=0.001) DRKYR (p=0.072)
Officer	0.89 (0.39,2.01)	0.776	
Enlisted Flyer	0.84 (0.29,2.43)	0.753	
Enlisted Groundcrew	1.59 (0.78,3.23)	0.205	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 11-33. (Continued)
Analysis of Gait

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent Abnormal**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	174	2.9	1.10 (0.78,1.56)	0.598
Medium	173	2.3		
High	170	4.7		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**	**Covariate Remarks**
504	1.24 (0.86,1.80)**	0.260**	INIT*AGE (p=0.031) AGE*DRKYR (p=0.016)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table G-2-13 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 11-33. (Continued)
Analysis of Gait

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,061	3.5		
Background RH	373	3.8	1.16 (0.61,2.18)	0.655
Low RH	260	1.9	0.53 (0.20,1.36)	0.184
High RH	257	4.7	1.28 (0.66,2.51)	0.467
Low plus High RH	517	3.3	0.90 (0.50,1.62)	0.726

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,043			AGE (p=0.007) DRKYR (p=0.077)
Background RH	366	1.13 (0.60,2.14)	0.706	
Low RH	254	0.52 (0.20,1.35)	0.182	
High RH	250	1.48 (0.75,2.94)	0.259	
Low plus High RH	504	0.96 (0.53,1.73)	0.889	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 11-33. (Continued)
Analysis of Gait

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	3.4 (294)	3.3 (300)	3.7 (296)	1.01 (0.79,1.29)	0.945
5	3.0 (299)	3.7 (297)	3.7 (294)	1.02 (0.83,1.26)	0.854
6[c]	3.0 (298)	3.7 (297)	3.7 (294)	1.00 (0.80,1.26)	0.970

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	889	0.94 (0.71,1.24)	0.662	AGE (p=0.061) OCC (p=0.099) DIAB*INS (p=0.033)
5	889	0.96 (0.76,1.22)	0.753	AGE (p=0.060) OCC (p=0.107) DIAB*INS (p=0.033)
6[d]	888	0.95 (0.73,1.22)	0.673	AGE (p=0.061) OCC (p=0.101) DIAB*INS (p=0.033)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 11-34.
Analysis of Central Nervous System (CNS) Index

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***947***	***6.0***	***1.03 (0.72,1.47)***	***0.950***
	Comparison	***1,279***	***5.9***		
Officer	Ranch Hand	366	4.9	0.78 (0.43,1.43)	0.515
	Comparison	501	6.2		
Enlisted Flyer	Ranch Hand	162	6.8	1.06 (0.46,2.43)	0.999
	Comparison	202	6.4		
Enlisted Groundcrew	Ranch Hand	419	6.7	1.26 (0.74,2.13)	0.470
	Comparison	576	5.4		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	***1.03 (0.72,1.48)***	***0.875***	AGE ($p<0.001$)
Officer	0.80 (0.44,1.46)	0.465	RACE ($p=0.096$)
Enlisted Flyer	1.07 (0.46,2.47)	0.874	DRKYR ($p=0.009$)
Enlisted Groundcrew	1.26 (0.73,2.16)	0.413	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 11-34. (Continued)
Analysis of Central Nervous System (CNS) Index

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	174	4.0	1.10 (0.84,1.45)	0.501
Medium	172	6.4		
High	170	7.1		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
516	1.22 (0.92,1.62)	0.181	AGE (p=0.013)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 11-34. (Continued)
Analysis of Central Nervous System (CNS) Index

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,062	6.3		
Background RH	373	6.2	1.01 (0.62,1.65)	0.969
Low RH	259	4.2	0.64 (0.33,1.24)	0.185
High RH	257	7.4	1.16 (0.68,1.97)	0.589
Low plus High RH	516	5.8	0.89 (0.57,1.40)	0.622

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,044			AGE ($p<0.001$) DRKYR ($p=0.055$)
Background RH	366	0.98 (0.59,1.62)	0.940	
Low RH	253	0.64 (0.33,1.23)	0.181	
High RH	250	1.30 (0.75,2.26)	0.356	
Low plus High RH	503	0.88 (0.56,1.40)	0.593	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$ 10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$ 10 ppt.
Low (Ranch Hand): Current Dioxin $>$ 10 ppt, 10 ppt $<$ Initial Dioxin $\leq$ 143 ppt.
High (Ranch Hand): Current Dioxin $>$ 10 ppt, Initial Dioxin $>$ 143 ppt.

Table 11-34. (Continued)
Analysis of Central Nervous System (CNS) Index

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	6.5 (294)	4.3 (300)	7.1 (295)	1.00 (0.83,1.22)	0.959
5	5.4 (299)	5.4 (296)	7.1 (294)	1.03 (0.87,1.21)	0.721
6[c]	5.4 (298)	5.4 (296)	7.1 (294)	0.99 (0.83,1.18)	0.869

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	889	0.93 (0.75,1.16)	0.519	AGE (p=0.022) OCC*INS (p=0.035)
5	889	0.97 (0.81,1.17)	0.766	AGE (p=0.020) OCC*INS (p=0.036)
6[d]	888	0.92 (0.76,1.12)	0.407	AGE (p=0.028) OCC*INS (p=0.030)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

None of the Ranch Hand categories differed significantly from the Comparison group in the unadjusted and adjusted Model 3 analyses of the CNS index (Table 11-34(e,f): $p>0.18$ for all contrasts). The adjusted analysis contained the covariates age and lifetime alcohol history.

The unadjusted and adjusted results for Models 4 through 6 did not reveal a significant association between current dioxin and the CNS index (Table 11-34(g,h): $p>0.40$ for all analyses). Each of the adjusted analyses included age and an occupation-by-insecticide exposure interaction.

Longitudinal Analysis

Physical Examination Variables

Longitudinal analyses were conducted on two composite variables, the cranial nerve index without range of motion and the CNS index, to examine whether changes over time differed with respect to group membership (Model 1), initial dioxin (Model 2), and categorized dioxin (Model 3). Models 4, 5, and 6 were not examined in the longitudinal analyses because current dioxin is the measure of exposure in these models. Current dioxin changes over time and is not available for all participants for 1985 and 1992. For both variables, the longitudinal analyses investigated the differences between the 1985 examination and the 1992 examination to enhance comparability, because SCRF conducted both of these neurological examinations.

The longitudinal analyses examined relative risks at the 1992 examination for participants who were classified as "normal" at the 1985 examination. Participants classified as "abnormal" at the 1985 examination were excluded because the focus of the analyses was on investigating the temporal effects of dioxin during the period between 1985 and 1992. Participants classified as "abnormal" in 1985 were already abnormal before this period; consequently, only participants classified as "normal" at the 1985 examination were considered to be at risk when the effects of dioxin over time were explored. The rate of abnormalities under this restriction approximates an incidence rate between 1985 and 1992. All three models were adjusted for age; Models 2 and 3 also were adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

Cranial Nerve Index without Range of Motion

Based on participants with a normal response in 1985, the Model 1 analysis of the cranial nerve index without range of motion did not reveal a significant overall group difference (Table 11-35(a): $p=0.343$). However, stratifying the analysis by occupation revealed a significant group difference within the enlisted groundcrew stratum ($p=0.049$, Adj. RR=2.33, 95% C.I.=[1.00,5.41]) and a marginally significant group difference within the enlisted flyer stratum ($p=0.068$, Adj. RR=0.14, 95% C.I.=[0.02,1.16]. For the enlisted groundcrew, Ranch Hands were more than twice as likely as Comparisons to develop a cranial nerve index abnormality in 1992 conditioned on normality in 1985 (4.0% vs. 1.8%). By contrast, the enlisted flyer Ranch Hands were less than one fourth as likely as

the enlisted flyer Comparisons to have an abnormal cranial nerve index without range of motion response in 1992 conditioned on normality in 1985 (0.7% vs. 4.4%).

The Model 2 longitudinal analysis did not detect a significant association between initial dioxin and the cranial nerve index without range of motion (Table 11-35(b): $p=0.747$). Similarly, the longitudinal analysis of Model 3 did not find a significant difference between any of the Ranch Hands categories and the Comparison group (Table 11-35(c): $p>0.13$ for all contrasts).

CNS Index

The Model 1 analysis for participants with a normal CNS index in 1985 did not reveal a significant group difference based on the 1992 results (Table 11-36(a): $p>0.21$ for all contrasts).

For Model 2, the longitudinal analysis revealed a marginally significant positive association between initial dioxin and the CNS index (Table 11-36(b): $p=0.052$, Adj. $RR=1.41$, 95% C.I.$=[1.01,1.98]$). Based on the Ranch Hands in the Model 2 analysis who had a normal CNS index in 1985, the percentages of abnormalities in 1992 for the low, medium, and high initial dioxin categories were 2.5, 3.1, and 6.2 percent respectively.

The Model 3 longitudinal analysis found that Ranch Hands in the low dioxin category had significantly fewer CNS index abnormalities in 1992 than the Comparison group conditioned on normality in 1985 (Table 11-36(c): $p=0.042$, Adj. $RR=0.43$, 95% C.I.$=[0.19, 0.97]$). Based on participants with a normal CNS index in 1985, the percentages of participants that had a CNS index abnormality in 1992 were 2.9 percent of the low Ranch Hand category versus 5.6 percent of the Comparison group.

DISCUSSION

Although definitive diagnosis usually requires laboratory testing beyond the scope of the current study, the data analyzed in the neurological assessment can be relied upon to detect the presence, if not the cause, of neurological disease including disorders of the peripheral nervous system. CNS, cranial, and peripheral nerve variables examined can provide specific clues to the anatomical site of neurological lesions and clarify the need for additional diagnostic studies. Pertinent to the current study, the neurological examination is highly sensitive in detecting the presence of peripheral neuropathy, a suspect clinical condition related to TCDD exposure.

In clinical practice, it is convenient to divide the neurological assessment into examinations of the peripheral and cranial nerves. The 5 motor, and 4 sensory peripheral nerve variables and the 13 cranial nerve variables examined provide highly specific clues in the anatomic site of neurological lesions and clarify which additional diagnostic studies would be most helpful in establishing a diagnosis.

Table 11-35.
Longitudinal Analysis of Cranial Nerve Index without Range of Motion

a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Percent Abnormal/(n) Examination 1985	1987	1992
All	***Ranch Hand***	***3.7 (894)***	***4.4 (862)***	***4.8 (894)***
	Comparison	***2.3 (1,133)***	***4.0 (1,096)***	***3.3 (1,133)***
Officer	Ranch Hand	2.9 (345)	3.6 (337)	4.1 (345)
	Comparison	2.1 (435)	2.6 (420)	3.9 (435)
Enlisted Flyer	Ranch Hand	3.2 (158)	4.6 (154)	3.2 (158)
	Comparison	1.6 (187)	5.5 (181)	4.3 (187)
Enlisted Groundcrew	Ranch Hand	4.6 (391)	5.1 (371)	6.1 (391)
	Comparison	2.7 (511)	4.7 (495)	2.4 (511)

Occupational Category	Group	Normal in 1985: n in 1992	Percent Abnormal in 1992	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***861***	***3.4***	***1.29 (0.76,2.18)***	***0.343***
	Comparison	***1,107***	***2.6***		
Officer	Ranch Hand	335	3.9	1.37 (0.62,3.05)	0.439
	Comparison	426	2.8		
Enlisted Flyer	Ranch Hand	153	0.7	0.14 (0.02,1.16)	0.068
	Comparison	184	4.4		
Enlisted Groundcrew	Ranch Hand	373	4.0	2.33 (1.00,5.41)	0.049
	Comparison	497	1.8		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1985 and 1992 results; results adjusted for age in 1992.

Note: Summary statistics for 1987 are provided for reference purposes for participants who attended the 1985 and 1992 examinations. Statistical analyses are based only on participants who had a normal cranial nerve index without range of motion in 1985 (see Chapter 7, Statistical Methods).

Table 11-35. (Continued)
Longitudinal Analysis of Cranial Nerve Index without Range of Motion

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN			
	Percent Abnormal/(n) Examination		
Initial Dioxin	1985	1987	1992
Low	2.4 (165)	3.7 (162)	6.1 (165)
Medium	3.0 (166)	6.8 (162)	2.4 (166)
High	3.7 (164)	4.5 (156)	6.7 (164)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Normal in 1985			
Initial Dioxin	n in 1992	Percent Abnormal in 1992	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	161	5.6	0.94 (0.63,1.39)	0.747
Medium	161	1.2		
High	158	4.4		

[a] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of blood draw for dioxin, and age in 1992.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
Summary statistics for 1987 are provided for reference purposes for participants who attended the 1985 and 1992 examinations. Statistical analyses are based only on participants who had a normal cranial nerve index without range of motion in 1985 (see Chapter 7, Statistical Methods).

Table 11-35. (Continued)
Longitudinal Analysis of Cranial Nerve Index without Range of Motion

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY			
	Percent Abnormal/(n) Examination		
Dioxin Category	1985	1987	1992
Comparison	2.1 (980)	4.3 (960)	3.2 (980)
Background RH	4.6 (351)	3.5 (342)	4.6 (351)
Low RH	3.2 (247)	5.4 (242)	5.7 (247)
High RH	2.8 (248)	4.6 (238)	4.4 (248)
Low plus High RH	3.0 (495)	5.0 (480)	5.1 (495)

	Normal in 1985			
Dioxin Category	n in 1992	Percent Abnormal in 1992	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	959	2.5		
Background RH	335	3.0	1.16 (0.54,2.47)	0.702
Low RH	239	4.6	1.75 (0.84,3.66)	0.134
High RH	241	2.9	1.27 (0.54,3.03)	0.584
Low plus High RH	480	3.8	1.53 (0.82,2.87)	0.183

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of blood draw for dioxin, and age in 1992.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$10 ppt.
Low (Ranch Hand): Current Dioxin $>$10 ppt, 10 ppt $<$ Initial Dioxin $\leq$143 ppt.
High (Ranch Hand): Current Dioxin $>$10 ppt, Initial Dioxin $>$ 143 ppt.
Summary statistics for 1987 are provided for reference purposes for participants who attended the 1985 and 1992 examinations. Statistical analyses are based only on participants who had a normal cranial nerve index without range of motion in 1985 (see Chapter 7, Statistical Methods).

Table 11-36.
Longitudinal Analysis of Central Nervous System Index

a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Percent Abnormal/(n) Examination		
		1985	1987	1992
All	***Ranch Hand***	***4.0 (908)***	***5.9 (882)***	***6.1 (908)***
	Comparison	***2.7 (1,149)***	***4.7 (1,121)***	***5.7 (1,149)***
Officer	Ranch Hand	2.9 (351)	3.5 (343)	5.1 (351)
	Comparison	1.4 (443)	4.2 (431)	6.1 (443)
Enlisted Flyer	Ranch Hand	6.3 (158)	5.2 (154)	7.0 (158)
	Comparison	4.3 (188)	4.9 (184)	5.3 (188)
Enlisted Groundcrew	Ranch Hand	4.0 (399)	8.3 (385)	6.5 (399)
	Comparison	3.3 (518)	5.1 (506)	5.6 (518)

Occupational Category	Group	Normal in 1985		Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
		n in 1992	Percent Abnormal in 1992		
All	***Ranch Hand***	***872***	***4.1***	***0.78 (0.51,1.20)***	***0.252***
	Comparison	***1,118***	***5.2***		
Officer	Ranch Hand	341	3.8	0.64 (0.32,1.28)	0.212
	Comparison	437	5.7		
Enlisted Flyer	Ranch Hand	148	4.7	0.93 (0.34,2.58)	0.892
	Comparison	180	5.0		
Enlisted Groundcrew	Ranch Hand	383	4.2	0.87 (0.45,1.67)	0.679
	Comparison	501	4.8		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1985 and 1992 results; results adjusted for age in 1992.

Note: Summary statistics for 1987 are provided for reference purposes for participants who attended the 1985 and 1992 examinations. Statistical analyses are based only on participants who had a normal cranial nerve index without range of motion in 1985 (see Chapter 7, Statistical Methods).

Table 11-36. (Continued)
Longitudinal Analysis of Central Nervous System Index

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN

Initial Dioxin	Percent Abnormal/(n) Examination		
	1985	1987	1992
Low	3.6 (167)	2.4 (167)	4.2 (167)
Medium	3.0 (166)	4.9 (163)	5.4 (166)
High	3.0 (167)	8.0 (162)	7.2 (167)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Normal in 1985			
Initial Dioxin	n in 1992	Percent Abnormal in 1992	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	161	2.5	1.41 (1.01,1.98)	0.052
Medium	161	3.1		
High	162	6.2		

[a] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of blood draw for dioxin, and age in 1992.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
Summary statistics for 1987 are provided for reference purposes for participants who attended the 1985 and 1992 examinations. Statistical analyses are based only on participants who had a normal cranial nerve index without range of motion in 1985 (see Chapter 7, Statistical Methods).

Table 11-36. (Continued)
Longitudinal Analysis of Central Nervous System Index

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY			
	Percent Abnormal/(n) Examination		
Dioxin Category	1985	1987	1992
Comparison	2.6 (995)	4.9 (981)	6.1 (995)
Background RH	4.2 (360)	6.0 (350)	6.4 (360)
Low RH	2.8 (249)	2.0 (247)	4.4 (249)
High RH	3.6 (251)	8.2 (245)	6.8 (251)
Low plus High RH	3.2 (500)	5.1 (492)	5.6 (500)

	Normal in 1985			
Dioxin Category	n in 1992	Percent Abnormal in 1992	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	969	5.6		
Background RH	345	4.4	0.76 (0.42,1.37)	0.358
Low RH	242	2.9	0.43 (0.19,0.97)	0.042
High RH	242	5.0	1.02 (0.53,1.98)	0.943
Low plus High RH	484	3.9	0.68 (0.40,1.17)	0.166

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of blood draw for dioxin, and age in 1992.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$10 ppt.
Low (Ranch Hand): Current Dioxin >10 ppt, 10 ppt < Initial Dioxin $\leq$143 ppt.
High (Ranch Hand): Current Dioxin >10 ppt, Initial Dioxin > 143 ppt.
Summary statistics for 1987 are provided for reference purposes for participants who attended the 1985 and 1992 examinations. Statistical analyses are based only on participants who had a normal cranial nerve index without range of motion in 1985 (see Chapter 7, Statistical Methods).

As indices of CNS function, tremor and coordination are less specific and more subject to individual variation in the absence of underlying neurological disease. Tremor, for example, may occur as a benign familial trait, may be reflective of alcohol withdrawal, or may be a marker of extra pyramidal motor system disease as in Parkinson's Syndrome. The Romberg sign may signal a lesion in the cerebellum but is more often indicative of impaired position sense in the lower extremities or of inner ear disease. Finally, the mental status examination is of obvious importance in the CNS assessment and, as in previous examination cycles, extensive psychometric studies were conducted and are reported in Chapter 12, Psychology Assessment.

In the adjusted analyses of the medical records variables, the prevalence of neurological disorders by history was similar in the Ranch Hand and Comparison cohorts. In a pattern consistent with a positive dose-response and with results reported in the serum dioxin analysis of the 1987 followup, the diagnosis of other neurological disorders occurred more commonly in Ranch Hands with high versus medium and low levels of serum dioxin. After adjustment for covariates, however, the associations were no longer statistically significant. In contrast, but of doubtful clinical significance, an inverse dose-response was noted in all adjusted analyses relating the current serum dioxin to the history of hereditary and degenerative disorders. Disorders included in this ICD-9-CM category, more common in Ranch Hands than in Comparisons in the 1987 examinations, were equally prevalent in the current study.

In relation to the extrapolated initial level of serum dioxin, no significant associations were noted in the adjusted analyses of any of the directly measured physical examination variables. The analyses employing current serum dioxin yielded inconsistent results. A positive association was noted in relation to the cranial nerve motor variable smile and the peripheral nerve variables pin prick and patellar reflex, while inverse dose-response patterns were defined for smell and the Babinski reflex.

The dependent variable-covariate analyses confirmed associations well-established in clinical practice. Diabetes mellitus was associated with multiple motor and sensory manifestations of neurological disease including deficits in pin prick sensation and balance, the Romberg sign, and all of the deep tendon reflexes tested. Consistent with the peripheral neuropathy common to age, alcoholism, and diabetes, highly significant associations were noted between these risk factors and abnormalities in the vibrotactile threshold (of both left and right great toes).

In summary, data analyzed in the current section reflect a comparable prevalence of neurological disease in the Ranch Hand and Comparison cohorts and no consistent evidence for a dose-response effect in relation to the current body burden of dioxin.

SUMMARY

The neurological assessment focused on extensive physical examination data for cranial nerve function, peripheral nerve status, and CNS coordination processes. Verified histories of neurological diseases also were examined. Tables 11-37 through 11-40 summarize the results of the group contrast analyses (Table 11-37), the initial dioxin analyses (Table 11-38),

Table 11-37.
Summary of Group Analyses (Model 1) for Neurological Variables
(Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Medical Records				
Inflammatory Diseases (D)	NS	NS	NS	NS
Hereditary and Degenerative Diseases (D)	NS	NS	ns	NS
Peripheral Disorders (D)	NS	NS	NS	ns
Other Neurological Disorders (D)	NS	NS	NS	NS
Physical Examination: Cranial Nerve Function				
Smell (D)	NS	ns	NS	NS
Visual Fields (D)	ns	ns	--	NS
Light Reaction (D)	NS	ns	ns	NS*
Ocular Movement (D)	NS	NS	NS	NS
Facial Sensation (D)	NS	--	ns	NS
Jaw Clench (D)	--	--	--	--
Smile (D)	NS	ns	NS	NS
Palpebral Fissure (D)	ns	ns	NS	ns
Balance (D)	NS	NS	ns	NS
Gag Reflex (D)	--	--	--	--
Speech (D)	NS	NS	NS	NS
Palate and Uvula Movement (D)	--	--	--	--
Neck Range of Motion (D)	NS	NS	ns	NS
Cranial Nerve Index without Range of Motion (D)	NS	ns	ns	+0.012
Physical Examination: Peripheral Nerve Status				
Pin Prick (D)	NS	ns	ns	NS
Light Touch (D)	NS	NS	NS	NS
Muscle Status (D)	NS	NS	ns	NS
Patellar Reflex (D)	-0.043	-0.033	ns	NS
Achilles Reflex (D)	NS	NS	ns	ns
Biceps Reflex (D)	ns	NS	ns	ns
Babinski Reflex (D)	ns	ns	ns	NS
Vibrotactile Threshold Measurement of Right Great Toe (C)	NS	ns	NS	NS

Table 11-37. (Continued)
Summary of Group Analyses (Model 1) for Neurological Variables
(Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Vibrotactile Threshold Measurement of Left Great Toe (C)	NS	NS	ns	NS
Physical Examination: CNS Coordination Processes				
Tremor (D)	NS	ns	NS	NS
Coordination (D)	NS	NS	ns	NS
Romberg Sign (D)	NS	NS	ns	NS
Gait (D)	NS	ns	ns	NS
Central Nervous System Index (D)	NS	ns	NS	NS

C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00.
-: Relative risk < 1.00.
--: Analysis not performed due to sparse number of abnormalities.
NS or ns: Not significant ($p > 0.10$).
Note: P-value given if $p \leq 0.05$.
A capital "NS" denotes a relative risk 1.00 or greater for discrete analysis or difference of means nonnegative for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Table 11-37. (Continued)
Summary of Group Analyses (Model 1) for Neurological Variables
(Ranch Hands vs. Comparisons)

Variable	ADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Medical Records				
Inflammatory Diseases (D)	NS	NS	NS	NS
Hereditary and Degenerative Diseases (D)	NS	NS	ns	NS
Peripheral Disorders (D)	NS	NS	ns	ns
Other Neurological Disorders (D)	NS	NS	NS	NS
Physical Examination: Cranial Nerve Function				
Smell (D)	NS	ns	NS	NS
Visual Fields (D)	ns	ns	--	NS
Light Reaction (D)	NS	ns	--	--
Ocular Movement (D)	NS	NS	--	NS
Facial Sensation (D)	NS	--	ns	NS
Jaw Clench (D)	--	--	--	--
Smile (D)	NS	ns	NS	NS
Palpebral Fissure (D)	ns	ns	NS	ns
Balance (D)	NS	NS	--	NS
Gag Reflex (D)	--	--	--	--
Speech (D)	NS*	NS	--	NS
Palate and Uvula Movement (D)	--	--	--	--
Neck Range of Motion (D)	NS	NS	ns*	NS
Cranial Nerve Index without Range of Motion (D)	**(NS)	ns	ns	+0.014
Physical Examination: Peripheral Nerve Status				
Pin Prick (D)	ns	ns	ns	NS
Light Touch (D)	NS	ns	NS	NS
Muscle Status (D)	NS	NS	ns	NS
Patellar Reflex (D)	**(-0.009)	**(-0.021)	**(-0.048)	**(NS)
Achilles Reflex (D)	NS	NS	ns	ns
Biceps Reflex (D)	ns	NS	--	ns
Babinski Reflex (D)	ns	--	--	NS
Vibrotactile Threshold Measurement of Right Great Toe (C)	ns	ns	NS	NS
Vibrotactile Threshold Measurement of Left Great Toe (C)	NS	ns	ns	NS

Table 11-37. (Continued)
Summary of Group Analyses (Model 1) for Neurological Variables
(Ranch Hands vs. Comparisons)

Variable	ADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Physical Examination: CNS Coordination Processes				
Tremor (D)	NS	ns	NS	NS
Coordination (D)	NS	NS	ns	NS
Romberg Sign (D)	NS	NS	--	NS
Gait (D)	NS	ns	ns	NS
Central Nervous System Index (D)	NS	ns	NS	NS

C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00.
-: Relative risk < 1.00.
--: Analysis not performed due to sparse number of abnormalities.
NS or ns: Not significant ($p > 0.10$).
NS* or ns*: Marginally significant ($0.05 < p \leq 0.10$).
**(NS) or **(ns): Group-by-covariate interaction ($p \leq 0.05$); not significant when interaction is deleted; refer to Appendix G-2 for further analysis of this interaction.
**(...): Group-by-covariate interaction ($p \leq 0.05$); significant when interaction is deleted and p-value is given in parentheses; refer to Appendix G-2 for further analysis of this interaction.
Note: A capital "NS" denotes a relative risk 1.00 or greater for discrete analysis or difference of means nonnegative for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Table 11-38.
Summary of Initial Dioxin Analyses (Model 2) for Neurological Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Medical Records		
Inflammatory Diseases (D)	NS	ns
Hereditary and Degenerative Diseases (D)	ns	**(ns)
Peripheral Disorders (D)	NS	NS
Other Neurological Disorders (D)	NS	ns
Physical Examination: Cranial Nerve Function		
Smell (D)	ns	ns
Visual Fields (D)	--	--
Light Reaction (D)	NS	NS
Ocular Movement (D)	ns	ns
Facial Sensation (D)	NS	--
Jaw Clench (D)	--	--
Smile (D)	NS	NS
Palpebral Fissure (D)	NS	NS
Balance (D)	NS	NS
Gag Reflex (D)	--	--
Speech (D)	NS	NS
Palate and Uvula Movement (D)	--	--
Neck Range of Motion (D)	ns	NS
Cranial Nerve Index without Range of Motion (D)	NS	**(NS)
Physical Examination: Peripheral Nerve Status		
Pin Prick (D)	ns	ns
Light Touch (D)	ns	ns
Muscle Status (D)	ns	NS
Patellar Reflex (D)	ns	NS
Achilles Reflex (D)	ns	**(NS)
Biceps Reflex (D)	-0.030	ns
Babinski Reflex (D)	--	--
Vibrotactile Threshold Measurement of Right Great Toe (C)	ns	**(NS)
Vibrotactile Threshold Measurement of Left Great Toe (C)	ns*	**(NS)

Table 11-38. (Continued)
Summary of Initial Dioxin Analyses (Model 2) for Neurological Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Physical Examination: CNS Coordination Processes		
Tremor (D)	NS	NS
Coordination (D)	ns	NS
Romberg Sign (D)	NS	NS
Gait (D)	NS	**(NS)
Central Nervous System Index (D)	NS	NS

C: Continuous analysis.
D: Discrete analysis.
-: Relative risk < 1.00.
--: Analysis not performed due to sparse number of abnormalities.
NS or ns: Not significant ($p > 0.10$).
ns*: Marginally significant ($0.05 < p \leq 0.10$).
**(NS) or **(ns): Log_2 (initial dioxin)-by-covariate interaction ($p \leq 0.05$); not significant when interaction is deleted; refer to Appendix G-2 for further analysis of this interaction.
Note: P-value given if $p \leq 0.05$.
A capital "NS" denotes a relative risk 1.00 or greater for discrete analysis or slope nonnegative for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or slope negative for continuous analysis.

Table 11-39.
Summary of Categorized Dioxin Analyses (Model 3) for Neurological Variables (Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Medical Records				
Inflammatory Diseases (D)	NS	NS	NS	NS
Hereditary and Degenerative Diseases (D)	NS	NS	ns	NS
Peripheral Disorders (D)	ns	NS	NS	NS
Other Neurological Disorders (D)	ns	NS	+0.040	NS*
Physical Examination: Cranial Nerve Function				
Smell (D)	NS	NS	ns	ns
Visual Fields (D)	--	--	--	--
Light Reaction (D)	NS	NS	NS	NS*
Ocular Movement (D)	NS	NS	NS	NS
Facial Sensation (D)	NS	--	NS*	NS
Corneal Reflex (D)	--	--	--	--
Jaw Clench (D)	--	--	--	--
Smile (D)	NS	NS	NS	NS
Palpebral Fissure (D)	NS	NS	ns	NS
Balance (D)	NS	ns	NS	NS
Gag Reflex (D)	--	--	--	--
Speech (D)	NS	NS*	NS*	+0.023
Tongue Position Relative to Midline (D)	--	--	--	--
Palate and Uvula Movement (D)	--	--	--	--
Neck Range of Motion (D)	NS	NS	NS	NS
Cranial Nerve Index without Range of Motion (D)	NS	NS	NS	NS
Physical Examination: Peripheral Nerve Status				
Pin Prick (D)	ns	NS	ns	NS
Light Touch (D)	NS	NS	NS	NS
Muscle Status (D)	NS	NS	NS	NS
Patellar Reflex (D)	-0.033	ns	ns	ns
Achilles Reflex (D)	NS	NS	ns	NS
Biceps Reflex (D)	ns	NS	ns	ns
Babinski Reflex (D)	ns	ns	ns	ns

Table 11-39. (Continued)
Summary of Categorized Dioxin Analyses (Model 3) for Neurological Variables (Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Vibrotactile Threshold Measurement of Right Great Toe (C)	ns	NS	ns	NS
Vibrotactile Threshold Measurement of Left Great Toe (C)	NS	NS	ns	NS
Physical Examination: CNS Coordination Processes				
Tremor (D)	NS	ns	NS	ns
Coordination (D)	ns	NS	NS	NS
Romberg Sign (D)	NS	ns	NS	NS
Gait (D)	NS	ns	NS	ns
Central Nervous System Index (D)	NS	ns	NS	ns

C: Continuous analysis.
D: Discrete analysis.
+: Relative risk $\geq$ 1.00 for discrete analysis or difference of means nonnegative for continuous analysis.
-: Relative risk $<$ 1.00 for discrete analysis or difference of means negative for continuous analysis.
--: Not applicable for unadjusted analysis.
NS or ns: Not significant ($p > 0.10$).
NS*: Marginally significant ($0.05 < p \leq 0.10$).
Note: P-value given if $p \leq 0.05$.
A capital "NS" denotes a relative risk 1.00 or greater for discrete analysis or difference of means nonnegative for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Table 11-39. (Continued)
Summary of Categorized Dioxin Analyses (Model 3) for Neurological Variables (Ranch Hands vs. Comparisons)

Variable	ADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Medical Records				
Inflammatory Diseases (D)	NS	NS	NS	NS
Hereditary and Degenerative Diseases (D)	NS	NS	ns	ns
Peripheral Disorders (D)	ns	ns	NS	NS
Other Neurological Disorders (D)	NS	NS	NS	NS
Physical Examination: Cranial Nerve Function				
Smell (D)	**(NS)	**(NS)	**(ns)	**(ns)
Visual Fields (D)	--	--	--	--
Light Reaction (D)	NS	NS	NS	NS*
Ocular Movement (D)	NS	NS	NS	NS
Facial Sensation (D)	--	--	--	--
Corneal Reflex (D)	--	--	--	--
Jaw Clench (D)	--	--	--	--
Smile (D)	NS	NS	NS	NS
Palpebral Fissure (D)	NS	NS	ns	NS
Balance (D)	NS	ns	NS	NS
Gag Reflex (D)	--	--	--	--
Speech (D)	--	--	--	--
Tongue Position Relative to Midline (D)	--	--	--	--
Palate and Uvula Movement (D)	--	--	--	--
Neck Range of Motion (D)	**(ns)	**(NS)	**(NS)	**(NS)
Cranial Nerve Index without Range of Motion (D)	**(NS)	**(NS)	**(NS)	**(NS)
Physical Examination: Peripheral Nerve Status				
Pin Prick (D)	ns	NS	ns	NS
Light Touch (D)	NS	NS	NS	NS
Muscle Status (D)	**(NS)	**(NS)	**(NS)	**(NS)
Patellar Reflex (D)	**(-0.025)	**(ns*)	**(ns)	**(ns)
Achilles Reflex (D)	**(NS)	**(NS)	**(NS)	**(NS)

Table 11-39. (Continued)
Summary of Categorized Dioxin Analyses (Model 3) for Neurological Variables (Ranch Hands vs. Comparisons)

Variable	ADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Biceps Reflex (D)	--	NS	ns	ns
Babinski Reflex (D)	ns	ns	--	ns
Vibrotactile Threshold Measurement of Right Great Toe (C)	**(ns)	**(ns)	**(NS)	**(NS)
Vibrotactile Threshold Measurement of Left Great Toe (C)	ns	NS	NS	NS
Physical Examination: CNS Coordination Processes				
Tremor (D)	NS	ns	NS	ns
Coordination (D)	ns	NS	NS	NS
Romberg Sign (D)	NS	ns	NS	NS
Gait (D)	NS	ns	NS	ns
Central Nervous System Index (D)	ns	ns	NS	ns

C: Continuous analysis.
D: Discrete analysis.
-: Relative risk <1.00 for discrete analysis or difference of means negative for continuous analysis.
--: Not applicable for unadjusted analysis.
NS or ns: Not significant ($p>0.10$).
NS* or ns*: Marginally significant ($0.05<p\leq0.10$).
**(NS) or **(ns): Categorized dioxin-by-covariate interaction ($0.01<p\leq0.05$); not significant when interaction is deleted; refer to Appendix G-2 for further analysis of this interaction.
**(ns*): Categorized dioxin-by-covariate interaction ($0.01<p\leq0.05$); marginally significant when interaction is deleted; refer to Appendix G-2 for further analysis of this interaction.
**(...): Categorized dioxin-by-covariate interaction ($0.01<p\leq0.05$); significant ($p=-0.025$) when interaction is deleted; refer to Appendix G-2 for further analysis of this interaction.
Note: P-value given if $p\leq0.05$.
A capital "NS" denotes a relative risk 1.00 or greater for discrete analysis or difference of means nonnegative for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Table 11-40.
Summary of Current Dioxin Analyses (Models 4, 5, and 6) for Neurological Variables (Ranch Hands Only)

Variable	UNADJUSTED		
	Model 4: Lipid-Adjusted Current Dioxin	Model 5: Whole-Weight Current Dioxin	Model 6: Whole-Weight Current Dioxin Adjusted for Total Lipids
Medical Records			
Inflammatory Diseases (D)	NS	NS	NS
Hereditary and Degenerative Diseases (D)	ns	ns	ns*
Peripheral Disorders (D)	NS	NS	NS
Other Neurological Disorders (D)	+0.022	NS*	+0.011
Physical Examination: Cranial Nerve Function			
Smell (D)	-0.018	-0.015	-0.019
Visual Fields (D)	--	--	--
Light Reaction (D)	NS	NS	NS
Ocular Movement (D)	NS	NS	NS
Facial Sensation (D)	NS	NS	NS
Jaw Clench (D)	--	--	--
Smile (D)	NS*	NS	NS*
Palpebral Fissure (D)	NS	NS	NS
Balance (D)	NS	NS	NS
Gag Reflex (D)	--	--	--
Speech (D)	NS	NS	NS
Palate and Uvula Movement (D)	--	--	--
Neck Range of Motion (D)	NS	NS	NS
Cranial Nerve Index without Range of Motion (D)	NS	NS	NS
Physical Examination: Peripheral Nerve Status			
Pin Prick (D)	NS*	NS*	NS*
Light Touch (D)	NS	NS	NS
Muscle Status (D)	ns	ns	NS
Patellar Reflex (D)	NS	NS	NS
Achilles Reflex (D)	NS	NS	NS
Biceps Reflex (D)	NS	NS	NS
Babinski Reflex (D)	ns*	ns	ns
Vibrotactile Threshold Measurement of Right Great Toe (C)	NS	NS	ns
Vibrotactile Threshold Measurement of Left Great Toe (C)	ns	ns	ns

Table 11-40. (Continued)
Summary of Current Dioxin Analyses (Models 4, 5, and 6) for Neurological Variables (Ranch Hands Only)

Variable	UNADJUSTED		
	Model 4: Lipid-Adjusted Current Dioxin	Model 5: Whole-Weight Current Dioxin	Model 6: Whole-Weight Current Dioxin Adjusted for Total Lipids
Physical Examination: CNS Coordination Processes			
Tremor (D)	ns	ns	ns
Coordination (D)	ns	ns	ns
Romberg Sign (D)	NS	NS	NS
Gait (D)	NS	NS	NS
Central Nervous System Index (D)	NS	NS	ns

C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00.
-: Relative risk < 1.00.
--: Analysis not performed due to sparse number of abnormalities.
NS or ns: Not significant ($p > 0.10$).
NS* or ns*: Marginally significant ($0.05 < p \leq 0.10$).
Note: P-value given if $p \leq 0.05$.
A capital "NS" denotes a relative risk 1.00 or greater for discrete analysis or slope nonnegative for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or slope negative for continuous analysis.

Table 11-40. (Continued)
Summary of Current Dioxin Analyses (Models 4, 5, and 6) for Neurological Variables (Ranch Hands Only)

Variable	ADJUSTED		
	Model 4: Lipid-Adjusted Current Dioxin	Model 5: Whole-Weight Current Dioxin	Model 6: Whole-Weight Current Dioxin Adjusted for Total Lipids
Medical Records			
Inflammatory Diseases (D)	NS	NS	NS
Hereditary and Degenerative Diseases (D)	-0.030	-0.033	-0.009
Peripheral Disorders (D)	**(NS)	**(NS)	**(NS)
Other Neurological Disorders (D)	ns	ns	ns
Physical Examination: Cranial Nerve Function			
Smell (D)	-0.018	-0.015	-0.019
Visual Fields (D)	--	--	--
Light Reaction (D)	NS	NS	NS
Ocular Movement (D)	NS	NS	NS
Facial Sensation (D)	NS	NS	NS
Jaw Clench (D)	--	--	--
Smile (D)	NS*	NS	NS*
Palpebral Fissure (D)	NS	NS	NS
Balance (D)	NS	NS	NS
Gag Reflex (D)	--	--	--
Speech (D)	NS	NS	NS
Palate and Uvula Movement (D)	--	--	--
Neck Range of Motion (D)	NS	NS	NS
Cranial Nerve Index without Range of Motion (D)	ns	ns	ns
Physical Examination: Peripheral Nerve Status			
Pin Prick (D)	**(NS)	**(NS)	**(NS)
Light Touch (D)	NS	NS	NS
Muscle Status (D)	NS	NS	NS
Patellar Reflex (D)	NS*	NS*	+0.039
Achilles Reflex (D)	NS	NS	NS
Biceps Reflex (D)	NS	NS	NS*
Babinski Reflex (D)	-0.039	ns*	ns*
Vibrotactile Threshold Measurement of Right Great Toe (C)	**(NS)	**(NS)	**(NS)
Vibrotactile Threshold Measurement of Left Great Toe (C)	**(NS)	**(NS)	**(NS)

Table 11-40. (Continued)
Summary of Current Dioxin Analyses (Models 4, 5, and 6) for Neurological Variables (Ranch Hands Only)

Variable	ADJUSTED		
	Model 4: Lipid-Adjusted Current Dioxin	Model 5: Whole-Weight Current Dioxin	Model 6: Whole-Weight Current Dioxin Adjusted for Total Lipids
Physical Examination: CNS Coordination Processes			
Tremor (D)	**(ns)	**(ns)	**(ns)
Coordination (D)	NS	NS	NS
Romberg Sign (D)	NS	NS	NS
Gait (D)	ns	ns	ns
Central Nervous System Index (D)	ns	ns	ns

C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00.
-: Relative risk < 1.00.
--: Analyses not performed due to sparse number of abnormalities.
NS or ns: Not significant ($p > 0.10$).
NS* or ns*: Marginally significant ($0.05 < p \leq 0.10$).
**(NS) or **(ns): Log_2 (current dioxin + 1)-by-covariate interaction ($p \leq 0.05$); not significant when interaction is deleted; refer to Appendix G-2 for further analysis of this interaction.
Note: P-value given if $p \leq 0.05$.
A capital "NS" denotes a relative risk 1.00 or greater for discrete analysis or a nonnegative slope for continuous analysis; a lower case "ns" denotes relative risk less than 1.00.

Table 11-41.
Summary of Group-by-Covariate and Dioxin-by-Covariate Interactions from Adjusted Analyses of Neurological Variables

Model	Variable	Covariate
1[a]	Cranial Nerve Index without Range of Motion	Occupation
	Patellar Reflex (D)	Lifetime Alcohol History
2[b]	Hereditary and Degenerative Diseases (D)	Occupation
	Cranial Nerve Index without Range of Motion (D)	Age, Diabetic Class
	Achilles Reflex (D)	Lifetime Alcohol History
	Vibrotactile Threshold Measurement of Right Great Toe (C)	Composite Exposure to Heavy Metals
	Vibrotactile Threshold Measurement of Left Great Toe (C)	Diabetic Class, Composite Exposure to Heavy Metals
	Gait (D)	Age
3[c]	Smell (D)	Insecticide Exposure
	Neck Range of Motion (D)	Occupation
	Cranial Nerve Index without Range of Motion (D)	Occupation
	Muscle Status (D)	Insecticide Exposure
	Patellar Reflex (D)	Lifetime Alcohol History
	Achilles Reflex (D)	Lifetime Alcohol History
	Vibrotactile Threshold Measurement of Right Great Toe (C)	Lifetime Alcohol History
4[d]	Peripheral Disorders (D)	Lifetime Alcohol History
	Pin Prick (D)	Diabetic Class
	Vibrotactile Threshold Measurement of Right Great Toe (C)	Lifetime Alcohol History, Composite Exposure to Heavy Metals
	Vibrotactile Threshold Measurement of Left Great Toe (C)	Lifetime Alcohol History, Diabetic Class, Worked With Vibrating Power Equipment or Tools
	Tremor (D)	Age
5[e]	Peripheral Disorders (D)	Lifetime Alcohol History
	Pin Prick (D)	Diabetic Class
	Vibrotactile Threshold Measurement of Right Great Toe (C)	Lifetime Alcohol History, Composite Exposure to Heavy Metals
	Vibrotactile Threshold Measurement of Left Great Toe (C)	Lifetime Alcohol History, Worked With Vibrating Power Equipment or Tools
6[f]	Peripheral Disorders (D)	Lifetime Alcohol History
	Pin Prick (D)	Diabetic Class
	Vibrotactile Threshold Measurement of Right Great Toe (C)	Lifetime Alcohol History, Composite Exposure to Heavy Metals
	Vibrotactile Threshold Measurement of Left Great Toe (C)	Lifetime Alcohol History, Worked With Vibrating Power Equipment or Tools

C: Continuous analysis.
D: Discrete analysis.
[a] Group Analysis (Ranch Hands vs. Comparison).
[b] Ranch Hands—Log_2 (Initial Dioxin).
[c] Categorized Dioxin.
[d] Ranch Hands—Log_2 (Current Lipid-Adjusted Dioxin + 1).
[e] Ranch Hands—Log_2 (Current Whole-Weight Dioxin + 1).
[f] Ranch Hands—Log_2 (Current Whole-Weight Dioxin + 1), Adjusted for Total Lipids.

the categorized dioxin analyses (Table 11-39), and the current dioxin analyses (Table 11-40). Table 11-41 lists the group-by-covariate and dioxin-by-covariate interactions that were encountered in the adjusted analyses of the variables.

Medical Records

Historical data collected at the 1982, 1985, and 1987 examinations were updated with information collected at the 1992 health interview and grouped by ICD code into four categories of neurological disorders for analysis: inflammatory disorders (ICD-9 codes 3200-3269), hereditary and degenerative disorders (ICD-9 codes 3300-3379), peripheral disorders (ICD-9 codes 3501-3599), and other neurological disorders (ICD-9 codes 3400-3499). The category of other neurological disorders included mostly diagnoses of unspecified encephalopathy (73.2%).

Model 1: Group Analysis

The unadjusted and adjusted analyses found that the prevalence of neurological disorders did not differ significantly between the Ranch Hand and Comparison groups for any of the medical records variables. Although not significant, the estimated relative risk of inflammatory disease was more than 4.00. These results were affected by sparse data, as there were only six Ranch Hands and two Comparisons with a history of inflammatory disease.

Model 2: Initial Dioxin Analysis

Estimated initial dioxin exposure was not significantly associated with any of the historical neurological disorders in both the unadjusted and adjusted Model 2 analyses.

Model 3: Categorized Dioxin Analysis

The Ranch Hand dioxin category versus Comparison group contrasts were not significant for inflammatory diseases, hereditary and degenerative diseases, or peripheral disorders. The relative risk of the category of other neurological disorders was significantly greater than 1.00 in the unadjusted analysis for Ranch Hands in the high dioxin category, but this finding became nonsignificant after adjusting for age, race, and occupation. Occupation was highly associated with other neurological disorders and also is associated with dioxin exposure. Removing occupation from the adjusted model caused the relative risk to become significant.

Models 4 though 6: Current Dioxin Analysis

The unadjusted analyses of the category of other neurological disorders found a significant positive association with lipid-adjusted current dioxin in Model 4 and a marginally significant positive association with whole-weight dioxin in Model 5. The association with whole-weight dioxin became significant after forcing total lipids into the Model 6 analysis. Similar to the Model 3 results, all of these associations became nonsignificant after adjusting

for age, race, and occupation. The positive associations became highly significant when occupation was removed from the final adjusted models.

The unadjusted current dioxin analyses of hereditary and degenerative diseases were all nonsignificant, but the relative risks became significantly less than 1.00 in Models 4 through 6 after adjusting for covariates, including occupation and diabetic class. When occupation and diabetic class were removed from the final models, the adjusted results supported the unadjusted findings, revealing no significant associations.

The unadjusted and adjusted peripheral disorders results were not significant, but the adjusted relative risks became significantly greater than 1.0 after removing the occupation and diabetic class covariates from the final models. When current dioxin was adjusted for age only, the relative risks were significant, but the results became nonsignificant when adjusting for the age-by-occupation interaction in the final model. The diabetic class covariate (whether in or out) had minimal effect on the current dioxin significance level.

Physical Examination Variables

The neurological assessment analyzed 14 cranial nerve function variables (smell, visual fields, light reaction, ocular movement, facial sensation, jaw clench, smile, palpebral fissure, balance, gag reflex, speech, palate and uvula movement, neck range of motion, and a cranial nerve index), 9 peripheral nerve variables (pin prick, light touch, muscle status, vibrotactile threshold (of left and right great toes), patellar reflex, Achilles reflex, biceps reflex, and the Babinski reflex) and 5 CNS coordination process variables (tremor, coordination, Romberg sign (balance), gait, and a CNS summary index) with respect to group differences and associations with dioxin. There were few abnormalities for many of these variables, limiting the power to detect a significant difference.

Model 1: Group Analysis

There were no significant overall group differences for the cranial nerve function variables. However, the group contrasts stratified by occupation found that the adjusted relative risk of a cranial nerve index abnormality was significantly greater than 1.00 for enlisted groundcrew Ranch Hands ($p=0.014$, Adj. RR=2.36, 95% C.I.=[1.19,4.71]). Although not significant, the estimated relative risk was greater than 4.00 for facial sensation (3 Ranch Hands vs. 1 Comparison).

The unadjusted and adjusted analyses of the peripheral nerves found significantly fewer patellar reflex abnormalities in the Ranch Hand group than in the Comparison group ($p=0.009$, Adj. RR=0.40, 95% C.I.=[0.19,0.83]). Stratified by occupation, the adjusted relative risk of an abnormal patellar reflex was significantly less than 1.00 in the officer and enlisted flyer categories, and greater than 1.00, but not significant in the enlisted groundcrew category.

The overall group contrasts and the group contrasts stratified by occupation were not significant for the CNS coordination process variables.

Model 2: Initial Dioxin Analysis

The unadjusted Model 2 analyses found a significant negative association between biceps reflex and estimated initial dioxin exposure, but this finding became nonsignificant after adjustment for occupation. None of the other physical examination variables was associated significantly with initial dioxin exposure.

Model 3: Categorized Dioxin Analysis

There were significantly more Ranch Hands in the high dioxin category with facial sensation abnormalities and speech abnormalities than in the Comparison group ($p=0.008$, 0.8% vs. 0.0%). The percentage of speech abnormalities also was significantly greater in the low and low plus high Ranch Hand categories than in the Comparison group. The results from facial sensation and speech abnormalities must be interpreted with caution because, due to the sparse number of abnormalities, there was no adjustment for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin (incorporated to adjust for possible differential dioxin half-life elimination) or for any covariates. There also was a marginally significant increase in light reaction abnormalities for Ranch Hands in the low plus high dioxin category relative to the Comparison group. The only other significant finding in the unadjusted or adjusted Model 3 analyses was that the relative risk of patellar reflex abnormalities was significantly less than 1.00 for Ranch Hands in the background category.

Models 4 through 6: Current Dioxin Analyses

The unadjusted current dioxin analyses of the cranial nerve function variables found a significant inverse association with smell in Models 4, 5, and 6. The adjusted results were identical to the unadjusted findings because no covariates were retained in the final model. There were no significant associations between current dioxin and any of the other cranial nerve variables, although smile showed a marginally significant positive association with current dioxin in the unadjusted and adjusted Model 4 and 6 analyses.

The unadjusted analyses of the peripheral nerve status variables revealed marginally significant positive associations between current dioxin and pin prick in Models 4, 5, and 6, and a marginally significant inverse association between lipid-adjusted current dioxin and the Babinski reflex in Model 4.

The adjusted pin prick analyses yielded equivocal results. The associations with current dioxin (both lipid-adjusted and whole-weight) were not significant after adjustment for covariates, including occupation and diabetic class. However, the relative risks became significantly greater than 1.0 when occupation and diabetic class were removed from the model, and the current dioxin effect was adjusted only for age. In addition, the adjusted analyses showed a significant interaction between current dioxin and diabetic class in each of the adjusted analyses. Stratification of these interactions showed that the relative risk of a pin prick abnormality was significantly greater than 1.0 for diabetics, while the relative risks were not significant in both the normal and impaired strata.

After adjusting for age and occupation, the Babinski reflex analyses found a significant inverse relationship with lipid-adjusted current dioxin. The inverse association with whole-weight dioxin was marginally significant in Models 5 and 6.

The unadjusted current dioxin results for patellar reflex were not significant, but after adjusting for age, lifetime alcohol history, and diabetic class, the associations with lipid-adjusted dioxin in Model 4 and with whole-weight dioxin in Model 5 became marginally positive. The association with whole-weight dioxin became significantly positive in the adjusted Model 6 analysis, which forced total lipids into the model. When diabetic class was excluded from the final models, the association with lipid-adjusted current dioxin became significant, while the association with whole-weight dioxin remained marginally significant in Model 5 and significant in Model 6.

There were no significant associations between current dioxin and any of the CNS coordination process variables.

CONCLUSION

Overall, the neurological assessment found the prevalence of neurological disease to be comparable between the Ranch Hand and Comparison groups, and showed no consistent evidence of a dose-response effect with either estimated initial dioxin exposure or current TCDD levels. In the group contrasts stratified by occupation, Ranch Hand enlisted groundcrew, the occupation category with the highest current levels of dioxin, had significantly more cranial nerve index abnormalities than Comparison enlisted groundcrew, but the serum dioxin analyses did not find a significant dose-response.

For several variables—other neurological disorders, peripheral disorders, hereditary and degenerative diseases, neck range of motion, pin prick, light touch, vibrotactile threshold, biceps reflex and Babinski reflex—the results of the current dioxin models adjusted for the covariates occupation and diabetic class differed from results for followup models that removed these covariates. Possible explanations for differences include confounding, collinearity, differential half-life elimination associated with body fat measures related to diabetic class, and an indirect relationship between current dioxin and the dependent variable due to adjustment for diabetic class. Chapter 1, Introduction, and Chapter 7, Statistical Methods, contain Interpretive Considerations sections that discuss these issues in more detail.

The results for the category of other neurological disorders were primarily attributable to the confounding effects of occupation; enlisted personnel were three times as likely to have an other neurological disorder (mostly unspecified encephalopathy) than were officers. Thus more importance should be placed on the nonsignificant relative risks adjusted for occupation than on the significant relative risks that were not adjusted for occupation.

Interpretation of the results for some of the other variables becomes ambiguous because the diabetic class covariate is both a risk factor for the dependent variable and also is associated with body fat measures related to differential half-life elimination. The pin prick results are particularly difficult to interpret because in addition to the discrepant results between occupation and diabetic class (in and out of the model), each of the current dioxin

analyses found a significant interaction with diabetic class. The interactions displayed significant positive associations between current dioxin levels (lipid-adjusted and whole-weight) and pin prick for diabetics, but no significant association for participants classified as normal and impaired.

While the current dioxin analysis results for these variables may be unclear and inconclusive, they must be interpreted in conjunction with the other model results, which found no significant group differences and no significant associations with estimated initial dioxin (which was adjusted for differential half-life elimination).

CHAPTER 11
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